SCIENCE

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Contents

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

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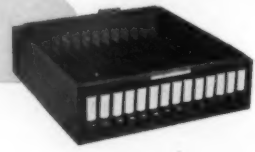

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The American Association for the Advancement of Science

THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE is an organization that has roughly fifty thousand individual members, and that represents affiliations with nearly two hundred scientific societies and academies. The Association has great potentialities for service to individual scientists, scientific groups, to science in general, and to our modern democratic society. It is the deep wish and the firm intention of the officers of the Association to do all in their power to help realize these potentialities.

To move forward with constructive and wise developments will require the best thinking of all the membership—hard and serious thinking, objective and loyal thinking. It will require imagination and the courage to run some risks in the attempt to serve great ends. We are confident that these qualities will be available to serve our Association.

In a situation such as ours, there is always danger that some members fear that changes will be too abrupt and too revolutionary, while many others are disappointed because there seems to be no progress. We ask for both confidence and patience. To the members of the first group we want to say that there is not, and never has been, so far as we know, any desire to bring about change that would be disruptive either in tempo or character. To the members of the second group we want to say that progress toward the Arden House goals is necessarily and properly slow; even though that progress has not become evident as yet, or in any event has not been publicly acclaimed, it is occurring.

Although it is the expressed will of the Association, as evidenced by the unanimous vote of the Council in favor of the Arden House policy, to alter, to modernize, and to enliven the annual meetings of the AAAS, we wish to caution that these changes should be worked out sensibly and gradually, proceeding by trial so that it can be assured that the meetings do in fact furnish that sort of inspiring contact with all of science which, we are sure, is desired by the membership.

In particular it is clear that for the time being it is important to include, at the big annual meeting, a certain body of short reports of current research in specialized fields. We bespeak, for our Association and, particularly, for the meeting in Boston this next winter, a full and active participation. We pledge that we will do our utmost to see to it that the Association, in all branches of its work, deserves your active support.

DETLEV W. BRONK, *Retiring President*
E. U. CONDON, *President*
WARREN WEAVER, *President-Elect*

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National Science Foundation Estimates for Scientific Research and Development

FEDERAL agencies spent $1839 million on scientific research and development during the fiscal year 1952. The corresponding estimate for the fiscal year 1953 is $2189 million. Amounts included in the President's Budget of January 9 for research and development total $2327 million for fiscal year 1954. These are preliminary estimates compiled by the National Science Foundation with the cooperation of other Federal agencies engaged in research and development activities. Estimates of obligations by Federal agencies for the same periods were also obtained.

This information was compiled by the Foundation in connection with its continuing studies of the research and development activities of the Federal Government. These reports will be of considerable value to many other Federal and private groups concerned in the administration and planning of Federal research and development programs.

Agencies reporting obligations and expenditures for research and development, in addition to the National Science Foundation, were Agriculture, Commerce, Defense, Interior, Labor, Post Office, State, and Treasury and the Atomic Energy Commission, Federal Civil Defense Administration, Federal Communications Commission, Federal Security Agency, Government Services Administration, Housing and Home Finance Agency, Interstate Commerce Commission, National Advisory Committee for Aeronautics, National Security Resources Board, Office of Defense Mobilization, Reconstruction Finance Corporation, Smithsonian Institution, Tariff Commission, Tennessee Valley Authority, and Veterans Administration.

TABLE 1

ESTIMATED OBLIGATIONS AND EXPENDITURES OF FEDERAL AGENCIES FOR SCIENTIFIC RESEARCH AND DEVELOPMENT IN FISCAL YEARS 1952, 1953, AND 1954*

(Millions of dollars)

Agency	Obligations†			Expenditures†		
	1952 (Actual)	1953 (Estimate)	1954 (Estimate)	1952 (Actual)	1953 (Estimate)	1954 (Estimate)
Department of Defense	1705	1850	1805	1315	1600	1700
Atomic Energy Commission	229	262	281	250	292	288
NACA	82	95	71	67	76	95
Department of Agriculture	56	66	61	57	60	69
Federal Security Agency	53	67	78	65	74	65
Department of Interior	36	36	39	33	37	39
Department of Commerce	31	23	39	28	24	39
Other agencies	25	28	37	24	26	32
Total‡	2216	2427	2411	1839	2189	2327

* Source: National Science Foundation.
† All amounts are given by fiscal years.
‡ Column items may not add to totals due to rounding.

Funds administered by the Department of Defense made up about 72 per cent of the total for 1952, compared with 14 per cent for the Atomic Energy Commission, 4 per cent for both the National Advisory Committee for Aeronautics and the Federal Security Agency. Twenty other Federal agencies accounted for the remaining funds. Similar ratios are indicated in the estimates for the fiscal years 1953 and 1954. The statistics indicate that $307 million was obligated in fiscal 1952 for increasing existing research facilities or construction of new laboratories. Of this sum, the Department of Defense accounted for $198 million, the Atomic Energy Commission for $80 million, and the National Advisory Committee for Aeronautics for $31 million.

The present available data are summarized in the accompanying table.

Physiologic Control of Fertility

Paul S. Henshaw

Planned Parenthood Federation of America, Inc., New York

PHYSIOLOGIC CONTROL of fertility in higher forms, including man, is feasible for the following reasons:

1) In normal life there are alternate periods of fertility and infertility; neither ovulation nor spermatogenesis occurs before puberty, and, in the female, ovulation occurs only once during each menstrual cycle, is suspended entirely during pregnancy, and occurs only rarely during lactation.

2) During the reproductive period of life individuals may swing from normal germ cell production to aspermia or anovulation and then return to normal production again.

3) Fertility is not essential for physical well-being, inasmuch as many individuals have active and satisfying lives without producing sperm or ova.

4) The reproductive system (male and female regarded as one) is complex and delicately balanced.

5) Specific events must occur in the pituitary, in the ovary, in the testis, in the oviducts, in the uterus, and in the vagina in a well-ordered sequence if reproduction is to occur.

6) At each of these points there is a physicochemical system of checks and balances which operate in a specific relation to each other to make the critical steps possible.

7) A slight shift to the right or to the left of center—center being the limits of tolerance of agents or conditions which will permit the critical events to occur—is sufficient to prevent certain of the events and thus break the chain.

8) Shifts to the right or to the left can be caused by providing more of normally occurring substances, or by adding antagonists to neutralize them.

For the purposes of this discussion it will be assumed that reproduction begins with action in the anterior pituitary. This organ is responsive to nervous and hormonal stimuli and secretes, among other agents, gonadotropins, of which there are at least two: follicle-stimulating hormone (FSH), and luteinizing hormone (LH). FSH, in the female, stimulates follicle growth, and, in the male, spermatogenesis. LH stimulates ovulation. There is interdependence between FSH and LH, but the relationship is understood in general outline only. In the young adult female several hundred thousand ova are present in the ovaries. Early in the menstrual cycle FSH, arriving by way of the blood, stimulates follicle growth; this action is followed by release of one or more ova at a time near the middle of the menstrual cycle.

In the adult human male, sperm are formed continuously in the testis at a rate depending in part upon available gonadotropins. Mature sperm accumulate in the epididymis. Sperm are expelled along with fluids from the prostate and other glands upon ejaculation, at which time the sperm become motile. The condition of the seminal fluid is critical with respect to acidity, viscosity, nutrient content, enzymes, and hormones; and the fluid must be of such character as to activate the sperm and nourish them during passage to meet the ovum in the Fallopian tubes.

The ovum before fertilization is surrounded by a cluster of ovarian cells, the corona radiata, which may gather certain tissue cement during the early period in the tubes. It is believed by some that these surrounding materials must be dispersed by enzymatic action before sperm can penetrate and fertilization can be achieved.

The fertilized ovum is moved along the tube by ciliary action and by muscular contraction of the tubes. Rate of passage in the tubes is critical, inasmuch as development must have proceeded to the proper stage when the embryo arrives in the uterus. Furthermore, condition of the tubular fluid is critical. This fluid must be suitable not only for sperm nourishment and passage, but also for nourishment and passage of the fertilized ovum moving in the opposite direction.

Upon arrival in the uterus the developing organism must have reached the blastocyst stage. If the walls of the uterus have been properly conditioned, and a trophoblast formed, the trophoblast adheres to the uterine wall, and these two parts grow to form the placenta.

During the growth of follicles in the ovaries, certain of the follicular cells secrete estrogen. When an ovum erupts from the ovary, the follicle becomes modified to form the corpus luteum, which secretes progesterone.

Estrogen and progesterone are master hormones. They exert influence resulting in preparation for important steps in the reproductive cycle. Estrogens, in the main, induce those conditions which insure fertilization; among other effects, they cause the tubes to form fluids favorable for passage and nourishment of sperm and fertilized ova. Progesterone and related compounds, on the other hand, tend to insure implantation. Under the influence of progesterone (after action by estrogens) the uterus becomes conditioned to receive the developing embryo. The placenta, when formed, takes up secretion of progesterone—a function, which, as will be seen, has significance in the control of ovulation.

Of basic significance is the fact that both estrogens and progesterone suppress pituitary secretion of gonadotropins—estrogen suppressing secretion of FSH and progesterone suppressing secretion of LH. Early in the menstrual cycle, when estrogen output is low, pituitary secretion of FSH is free, and a new wave of follicles is stimulated to develop. As a consequence, estrogen output begins to rise, and this, in turn, stimulates the pituitary to release LH, which stimulates release of an ovum from one (or more) of the follicles more advanced in development. With quick development of the corpus luteum and release of progesterone, LH is suppressed, and, as a consequence, no other ovulations occur during that particular cycle and partially developed follicles undergo atresia. As the result of both estrogen and progesterone secretion, changes occur in the uterus consisting of endometrial proliferation and glandular growth. If fertilization does not occur, this growth of tissues is unnecessary, and the endometrial layers are sloughed off at the time of the menstrual period. This cycle of events—consisting of the estrogenic and progestational phases—requires a period of approximately 28 days.

Of interest is the fact that ovulation sometimes fails to occur in some individuals during the 28-day cycle, and, in some, ovulation fails to take place at all. These conditions sometimes can be corrected by regulating hormone balance. Such facts justify the point of view that reproduction is dependent on a delicate system of checks and balances, and that a slight shift to the right or left at a critical time at certain locations will prevent reproduction without impairment to health, sexual vigor, or subsequent reproduction.

Two other points are of interest. The first, already mentioned, is that ovulation does not occur during pregnancy, because progesterone is secreted continuously by the placenta during pregnancy. The second is that in certain animals pseudo-pregnancy may occur as a result of sterile matings; the female in such cases experiences a period during which no ovulation occurs and several cycles are missed. This gives additional support to the view that ovulation can be controlled by shifts in the hormone balance.

Turning again to the male, it is known that a shift in the hormone balance will reduce or stop spermatogenesis entirely for limited periods of time, depending on the type and duration of treatment.

Control Approaches

During the past three decades, and particularly during the past few years, many papers have been published giving leads as to how fertility can be influenced or controlled by modification of conditions at one or another of the critical points. Some of the studies have been concerned specifically with the problem of control of fertility, but the majority have been devoted to other problems such as sterility, nutrition, immunology, cancer, and animal husbandry. We are aware of only three other attempts to bring together literature on this subject (*1–3*).

Agents or approaches for physiologic control of fertility may be grouped under general headings as follows: hormones, anti-hormones, anti-enzymes, immune bodies, modified media, symbiotic organisms, dietary factors, special agents, nervous stimuli, and rhythm (detection of ovulation). These topics will be considered in order, but it should be borne in mind that the listing of references in each case is representative rather than exhaustive.

I. *Hormones*:

General Developments. Evidence that fertility can be controlled by administration of hormonal agents became available as early as 1921, when Haberlandt (*4*) showed that the transplantation of ovaries from pregnant laboratory animals into mature females of the same species caused the latter to be sterile for limited periods. Haberlandt ascribed the result to the presence of corpus luteum hormone in the transplanted ovaries. Later Scaglione (*5*) observed that temporary sterility in female laboratory animals is produced by implantation of male gonads and by injection of testicular extracts. Parkes and Bellerby (*6*) injected corpus luteum extract into mice and rats and observed inhibition of ovulation and estrus for prolonged periods.

As early as 1937 Kurzrok (*7, 8*) set forth a clear prospectus for temporary hormonal sterilization. This author called attention to the fact that women in good health sometimes have sterile menstrual cycles—that is, cycles in which ovulation does not occur. Kurzrok pointed out that, when ovulation is absent, the corpus luteum fails to form and the endometrium retains its post-menstrual characteristics, but that bleeding occurs cyclically about every four weeks. He noted that anovulatory cycles are typical during lactation and stressed that the anovulatory cycle is one method by which the organism limits its own fertility. Novak (*9*) gave further recognition to the significance of anovulatory cycles in women.

Additional strength was given to the idea of hormonal control in 1927 when Frank (*10*) and Davis and Koff (*11*) showed that intravenous injection of pregnant mare's serum into anovulatory women would result in ovulation, fertilization, and pregnancy.

Editorials by Abraham Stone in the *Journal of Contraception* (*12*) and in *Human Fertility* (*13*) also set forth a picture of hormonal control of fertility.

Sturgis (*14*) reported a study of estrogen therapy for dysmenorrhea. On the assumption that dysmenorrhea is associated with ovulation and that ovulation can be prevented by administration of estrogen, the following information was found significant in relation to the problem of fertility control. If the first of a series of 6 to 12 injections was given within the first week after onset of the menses, the next period would invariably be free from uterine cramps, whereas, if the series was not started until two weeks after onset,

there was no alleviation at the time of the subsequent bleeding. These observations gave credence to the view that follicle growth can be suppressed by the administration of estrogens.

A study by Cole (*15*) was devoted to appraisal of the general principle of hormone regulation in the body and is typical of many since the concept of hormone control was first set forth. Cole brings together from various sources evidence showing that estrogens, progesterone, and androgens act to inhibit pituitary secretion of gonadotropins, thereby inhibiting follicular growth, ovulation, or spermatogenesis.

Sturgis (*16*), referring to the work of others, calls attention to the fact that there are around 400,000 ova in the ovaries of a young adult woman and that they undergo changes and disappear during the reproductive life. He also pointed out that, in the human cycle, usually only one egg escapes from the ovaries during each month, and that, since the reproductive span of a woman's life runs approximately from the twelfth to the fiftieth year, not more than 500 are released by one woman for potential fertilization and the others disappear by atresia. The picture developed by Sturgis stresses that, in the procession of developing follicles, there are first-rank follicles which mature and release ova, and second-rank follicles which undergo some development and then degenerate.

Evans *et al.* (*17*) demonstrated that purified lactogenic hormone will induce functional activity of corpora lutea. Since corpora lutea secrete progesterone, which in turn inhibits pituitary release of LH, it is clear why ovulation rarely occurs during lactation. Three articles by Byrnes and Meyer (*18–20*) indicate that in certain respects the effects of estrogen and progesterone are additive in inhibiting gonadotropic hormone secretion by the pituitary, and that the amounts of these agents required are small and within "physiologic" limits. These authors showed also that proportionately more estrogen is required to decrease FSH and to stimulate LH in the adolescent than in the adult and, on the basis of this observation, suggested that higher levels of FSH are an important factor in the attainment of sexual maturity.

Estrogens Alone. As early as 1932 Moore and Price (*21*) administered estrogen continuously to rats over a period of time and demonstrated that the gonadotropic potency of the pituitary is decreased. In the same year Meyer *et al.* (*22*) obtained similar results, also in rats. In 1937 Burdick and Whitney (*23*) injected 100 to 500 rat units of the estrogen progynon-B, causing acceleration of the rate of passage of ova through the Fallopian tubes of mice and a consequent condition of infertility. Whitney and Burdick (*24*) found that single injections of 5000 rat units of this estrogen given after ovulation result in accelerated tubal passage of the fertilized ova in rabbits, and that the developing ovum in the early cleavage stages disintegrates within a few hours after exposure to the uterine fluids; furthermore, they showed (*25*) that 100 to 500 rat units of progynon-B given to mice resulted in degeneration of the fertilized ova, the degeneration appearing to result from lack of proper sustaining fluid in the uterus, and not from the agent.

Parkes *et al.* (*26*) showed that small doses of ethinylestradiol or diethylstilbestrol administered by mouth prevent implantation of the blastocyst in the rabbit if given soon after ovulation, or they may terminate pregnancy. The effect of the agents, it is said, is produced in essentially a physiological manner; the luteal phase of the cycle is suppressed and another phase is induced, which, though not abnormal in itself, is unsuitable for development of the embryo. These authors state that everything we know about the menstrual cycle of primates suggests that its hormonal control is the same as in lower animals, and it is extremely probable that the factors governing implantation of the fertilized egg are fundamentally similar in women and in lower animals.

Hamblen *et al.* (*27*) administered diethylstilbestrol to women, giving doses of 2–6 mg per day on the fifth to the fourteenth or the twenty-fourth days of the menstrual cycle and observed marked variations in the length and duration of cycles and in amount of bleeding. These workers stated that the alterations were due in part to suppression of ovulation. Thompson (*28*) presented evidence showing that menstrual blood and dead endometrial cells contain a factor which stimulates pituitary release of FSH. Finnerty and Meyer (*29*) studied the effects of estrogen upon pituitary cytology and function and found a reduction in the gonadotropic content of the pituitary. They also found that the percentage of basophile cells in the pituitary was decreased in direct proportion to the concentration of estrogen administered. This, they pointed out, is evidence that the basophile cells of the pituitary are responsible for secretion of gonadotropins. The general picture is developed still further by Paschkis and Rakoff (*30*) in a study of the physiology of estrogenic hormones.

Progesterone Alone. Haberlandt (*31*) administered corpus luteum extracts intramuscularly or orally to laboratory animals and observed temporary sterility. Dempsey (*32*), in a study of reproductive activity in the guinea pig, showed that such widely differing experimental procedures as pregnancy, removal of corpora lutea, injection of progesterone, estrogen, testosterone, or androsterone benzoate do not influence the basic growth of follicles during the reproductive cycle, but that follicle growth is abolished completely by hypophysectomy; he concluded that progesterone inhibits pituitary release of LH.

Makepeace *et al.* (*33*) studied the effect of progestin and progesterone on ovulation in the rabbit and found that progesterone inhibited pituitary release of LH. Likewise, Astwood and Fevold (*34*) investigated the effect of progesterone on gonadotropic activity of the pituitary in rats and observed that this agent inhibited the release of LH.

Burdick (*35*) investigated the effect of progesterone

on ovaries and embryos of mice and determined that daily injections of 1 mg of this agent to female mice, starting on the day of mating, prevented implantation but that implantation was not prevented when the treatments were started one day later. This worker observed that embryos continued to grow during treatment but died within a few days after treatment was stopped. Corpora lutea were found to undergo regression during treatment.

Boyarsky *et al.* (*36*) administered progesterone to estrual rabbits for 10 days before experimental ovulation and observed a marked suppression of fertilization. Dutt and Casida (*37*) gave 5–10 mg of crystalline progesterone daily to ewes during the active mating season and found ovulation inhibited during the treatment period in all animals maintained on the larger dosages but in only part of those maintained on the smaller dosages. It was found, however, that estrus occurred in all animals 3 to 5 days after termination of treatment.

Ulberg *et al.* (*38*) studied the ovarian response in heifers to progesterone injections. They gave 50 mg daily and found that heat and ovulation were prevented if the treatments were started before heat occurred. Similar studies were carried out by Ulberg *et al.* (*39*) on gilts: 12.5, 25, 50, and 100 mg of progesterone per day were injected, and it was found that the larger doses inhibited heat and ovulation during the treatment period when injections were started early enough in the estrous cycle. Bradbury (*40*) administered 5-, 50-, and 100-mg doses of progesterone per day to human females and found that 20 mg per day for one week was usually sufficient to prevent menstruation.

Estrogen and Progesterone. Musser (*41*) stated that dysmenorrhea can be prevented in any cycle by preventing ovulation and that the administration of large daily doses of estrogen, beginning 4 days after the start of menstruation, will prevent ovulation. This author goes on to suggest that 1 mg of diethylstilbestrol could be given orally, beginning the first day of menstruation, in such a way as to have a fertility control effect, and that progesterone could be given to bring about menstruation.

Long and Bradbury (*42*) gave daily doses of 25 mg of progesterone plus 2.5 mg of estrogen to women and found a delay of menstruation of 3 to 6 weeks which was accompanied by decidual changes induced in the endometrium. Doses of 10 mg of progesterone plus 1 mg of estrogen, 25 mg of progesterone alone, or 2–5 mg of estrogen alone did not have these effects.

Androgen Alone. Burdick *et al.* (*43*) administered large doses of testosterone propionate to female mice and observed rapid passage of ova through the oviducts followed by failure of implantation.

Ludwig (*44*) showed that low doses of testosterone propionate suppressed pituitary secretion of gonadotropins, with consequent loss of sperm formation in laboratory animals, and that high doses, while they likewise inhibited the pituitary, resulted in a level of androgen which stimulates the seminiferous tubules directly.

Heckel *et al.* (*45, 46*) administered testosterone propionate (50 mg three times per week) to men and observed a fall in sperm count which approached zero level in a matter of days and which was maintained as long as the treatment was continued. In the work described the aspermic conditions were maintained as long as 3 months or more. After cessation of treatment recovery of sperm production occurred rapidly and sometimes reached levels higher than previously existed ("rebound" phenomena).

These observations add strength to the view that testosterone and estrogen produce effects in the male or in the female which are similar, and also to the view that rate of passage of developing ova through the oviducts is critical.

Other Agents — Prolactin, Hormone-Metabolites. Dresel (*47*) administered prolactin to mature nonparous mice and found the estrous cycle to be suspended for about 3 weeks. Similarly Lahr and Riddle (*48*) showed temporary suppression of ovarian cycles in rats and mice with prolactin.

Hisaw and Velardo (*49*) studied the action of pregnanediol (non-estrogenic fraction), which is one of the end products of progesterone metabolism, and found, in case of the decidual reaction in rats, that the agent was antagonistic to progesterone. This agent is of interest inasmuch as it is an end product of progesterone metabolism and accordingly would not be expected to exert the multiplicity of physiological effects that would be exerted by progesterone or by estrogen. Being an antagonist of progesterone, it may be expected to interrupt fertility by prevention of endometrial growth and perhaps by other means.

II. *Anti-hormones*:

Gonadotropins are protein in character and accordingly may be expected to induce antibody formation when used as antigens. Parkes and Rowlands (*50*) studied the inhibition of ovulation in the rabbit, using anti-gonadotropic serum. They found that such serum, obtained by prolonged injection of rabbits with ox anterior pituitary extract, inhibited the ovulation-producing activity of the antigenic extract itself. When the serum was administered intravenously to rabbits immediately after mating, ovulation, which ordinarily would have occurred in 10 to 12 hours, did not occur.

Gegerson (*51*) made similar studies in rabbits and obtained positive precipitin reactions. These authors were inclined, however, to believe that the inhibiting substance was separate and distinct from the anti-protein substances obtained. Thompson (*52*) presents an even more extended study and review.

Deutsch *et al.* (*53*) determined the time of appearance of the properties of anti-gonadotropic and progonadotropic substances of rat serum. Sera were obtained which had pro- and anti-gonadotropic effects in rabbits that had been injected with sheep pituitary extracts over prolonged and varying periods of time.

Jungck and Brown (*54*) administered gonadotropins to anovulatory females, with the hope of stimulating ovulation. The gonadotropins used were of animal origin, and the patients soon developed an immunity reaction to the agents being used, with the consequence that the agents were relatively ineffective in inducing ovulation.

III. *Anti-enzymes*:

In 1950 Meyer and McShan (*55*) made an extensive study (157 references) of hormone-enzyme relationships. They pointed out that changes in concentration of enzymes occur in tissues and organs under the influence of hormones, and that the enzyme value of organs and organelles should be interpreted in terms of enzyme levels in those organelles.

Many enzymes are involved in the reproductive process, but, so far as is known, attempts to develop an anti-enzyme which would break a link in the reproductive chain have been carried out in relation to only one enzyme—hyaluronidase, which is present at higher levels in semen.

McLean and Rowlands (*56*) demonstrated that bull testis hyaluronidase causes dispersion of the coronal cells surrounding recently ovulated mammalian ova. Fekete and Duran-Reynals (*57*) extended the study, pointing out that crude or highly purified preparations, known to be rich in hyaluronidase (extracts from rattlesnake venom, leech tissues, and testicles), have a very pronounced effect in dispersing the follicular cells surrounding the ova of mice. Later, Leonard and Kurzrok (*58*) demonstrated dispersion of coronal cells surrounding recently ovulated mammalian ova with bull testis hyaluronidase. Four papers (*59–62*) indicate that normal human seminal fluid contains higher levels of hyaluronidase. Six other papers (*63–68*) show that hyaluronidase content of semen is roughly proportional to the sperm count. Greenberg and Gargill (*69*) and Chang (*70*) raise questions about whether hyaluronidase is carried exclusively by the sperm, pointing out the possibility that seminal fluid may carry this substance. Kurzrok (*67*) stressed that the motility of sperm is in no way related to their hyaluronidase content. Kurzrok attempted to utilize hyaluronidase to overcome sterility in human males but without significant success.

Perlman *et al.* (*71*) were able to demonstrate that the level of hyaluronidase in the medium surrounding rat testis suspensions was increased by subjecting the cells to adverse treatments, such as freezing, incubation, and toluene. Pincus *et al.* (*72*) showed that hyaluronidase inhibitors may be used in rabbits to prevent the follicle cell dispersing activity of sperm hyaluronidase, thereby preventing fertilization.

Chang (*73*) raised an additional question about the actual importance of hyaluronidase *in vivo*, since in the clinical studies application of hyaluronidase in human infertility gave generally negative results.

Martin and Beiler (*74*) used phosphorylated hesperidin, a hyaluronidase inhibitor (20 mg/kg when given intraperitoneally, or 100 mg/kg when given orally) and found litter size and number of litters in rats markedly reduced.

Of particular interest is the fact that Sieve (*75*) has used phosphorylated hesperidin in human beings (300 couples) for the specific purpose of fertility control, and he reports clear-cut, positive results. Three times daily 100–200 mg of phosphorylated hesperidin in tablet form was given orally to both males and females. Ten days were allowed for the substance to reach saturation in both the man and the woman, after which no other contraceptive protection was utilized. The period of protection among the 300 couples varied from 3 to 30 months, and 220 couples bore normal offspring after termination of use of the agent. Only two couples developed pregnancies during the periods of intended protection, and each of these admitted negligence in maintaining saturation of the agent.

IV. *Immune Bodies*:

Attempts have been made to employ the principles of both passive and active immunity in the control of fertility.

Passive Immunity. The information available is given under anti-hormones above. It is evident that immune bodies can be developed which act antagonistically to gonadotropins, but, since constant application would be required to counteract continuous secretion of gonadotropins by the pituitary, it is doubtful that this approach will be significant from a practical point of view.

Active Immunity. Spermatotoxins: Many workers have held the view that immune bodies could be produced in the female of a given species by using sperm from the same or other species as an antigen to cause sperm to become ineffective upon deposit in the female.

The most direct work thus far performed for physiologic control of fertility has utilized the principle of active immunity. Our bibliography contains sixteen references indicating positive findings of one kind or another (*76–91*). About half of these deal with studies in human beings. More recently Henle and co-workers (*92–95*), and Parsons and Hyde (*96*), using pure strain animals and carefully devised immunological techniques, have obtained negative results, thus raising the question of the reliability of previous findings. Of interest would be work with males to reduce the effectiveness of sperm.

Wharton's Jelly. Langer (*97, 98*) utilized crude extracts of Wharton's Jelly as an antigen, attempting to produce immune bodies in female rats and mice against the formation of embryonic tissues, and found a significant reduction in number of litters and litter size.

V. *Modified Media*:

Cervical Mucus. The fluid content of the uterus is complex, and its requirements for reproduction are specific within narrow limits. It must be favorable for

the transport of sperm and also for support and maintenance of the blastocyst for a limited period. Cervical mucus is made up of secretions from the cervical glands, contributions from the oviduct, and probably also from materials drawn up from the vagina at the time of coitus. The mucus is comprised of a vast array of substrate materials, enzymes, hormones, steroids, and other special agents. Concentration, viscosity, and acidity are critical. The complexity of cervical mucus and the need for information with respect to the physiology of the uterus have been indicated by several authors (*99–109*).

Pommerenke observed that, at mid-cycle in human beings, the cervical mucus is increased in amount, acellularity, water content, and fluidity, and that, at this time, it is well supplied with carbohydrates and, presumably, amino acids. Pommerenke emphasizes that, because of these conditions, the sperm, on deposit in the vagina, must find an environment propitious for their nutrition and migration through the cervical canal. As has been pointed out above, these conditions are the consequence of estrogenic action. This author studied the effects of various hormones on recently castrated women. An estrogen product was found to stimulate cervical mucus secretion, which occurs at mid-cycle in normal subjects, whereas progesterone had no effect. The studies of Hughes (*103, 104*) furnish evidence that spontaneous abortion in human females can often be traced to a poorly functioning endometrium. His studies also show that, by means of therapeutic procedures designed to improve the functional qualities of the endometrium, women with a previous history of several abortions can achieve successful deliveries. Although the potentialities for control of fertility by modification of the cervical mucus are very great, no *in vivo* attempts have been made, so far as is known, to modify this complex physiology to reduce the probability of fertility.

Tubular Fluids. Much of what has been said about the physiologic complexity of the cervical mucus is also true of the tubular fluids. Burdick *et al.* (*110*) have shown that, if the tubes are distended by hormone stimulation so that the ovum cannot move at the appropriate rate, aging proceeds too rapidly in relation to the progress made and as a consequence implantation does not occur.

Semen. The physiologic condition of semen is similar to that of the cervical mucus and the fluid of the tubes. Concentration of substrate materials, pH, viscosity, enzymes, and hormone content are important, and the conditions of all must be maintained within narrow limits. Mann (*111–113*) has carried out extensive studies on metabolism of semen. He gives 336 references (*114*).

Bishop and Mathews (*115*) have shown an interesting inhibition of sperm motility by tetrazolium salts. They state that it is justifiable to conclude that the tetrazolium effect on sperm motility is not merely a reduction accompanying dehydrogenase activity, but is a physiological inhibition of a different order.

VI. *Symbiotic Organisms*:

Carter and Jones (*116*) and Matthews and Buxton (*117*) have made studies of the bacterial flora in the vagina and uterus of the human female. Their evidence indicates that some of the organisms must be responsible for infertility, inasmuch as treatment with antibiotics and elimination of certain of the species result in pregnancy. These observations suggest the possibility of organisms which can be transmitted from one individual to another for the purpose of preventing conception. The problem then would be merely one of elimination of the organisms by antibiotics for periods when conception is desired. Techniques are already known for accomplishment of this result.

VII. *Dietary Factors*:

Much evidence indicates that reproduction is affected by the presence or absence of specific factors in the diet. The seat of action, however, is often difficult to identify, because the presence or absence of dietary elements may cause modifications at several points.

With respect to inanition, Mason (*118*) and Ball *et al.* (*119*) studied the effects of starvation in rats and mice, respectively, and Smith (*120, 121*) observed the effects on human beings in Holland during World War II. In all three studies fertility was reduced, but the reduction was apparently due to simple lack of nourishment throughout the entire body.

In 1927 Evans and Burr (*122*) demonstrated that successful reproduction is dependent upon the fat-soluble vitamin E. Barrie (*123*) administered vitamin-E-deficient diets to rats and observed interruption of gestation. Evans (*124*) and Mason (*125*) observed fetal death, prolonged gestation, and difficult parturition in the rat as a result of vitamin A deficiency.

Holt *et al.* (*126*) maintained three male subjects on a diet deficient in arginine for 10 days. On the ninth day the seminal plasma of these subjects revealed a reduction in number of spermatozoa to approximately 1/10 normal. A similar diet containing arginine, which followed the deficiency period, resulted in slow return of sperm number to the normal level. Hertz (*127*) demonstrated dietary impairment of estrogen response in immature monkeys. Samuels (*128*) has extensively reviewed dietary factors in relation to hormones.

Gassner *et al.* (*129*) fed a ration of 70 per cent sesame meal to cockerels during the second to fourth weeks of age and found testicular degeneration accompanied by decrease of comb growth. Supplementation of this diet with vitamin B_{12} produced testicular growth, differentiation, and comb development equal to, or greater than, those in controls. Since the failure of growth and development observed was characteristic of that seen after pituitary failure to produce adequate gonadotropins, there is the possibility that vitamin B_{12} is required for pituitary function.

Kendall *et al.* (*130*) observed sterility in rabbits fed on soy bean hay, and, on the basis of other experiments, the enzyme lipoxidase was suspected of being

responsible. Nelson *et al.* (*131–133*), Hertz and Tullner (*134*) and Thiersch and Philips (*135*) have shown that tissue growth, including embryonic growth, is quantitatively dependent upon folic acid, and that anti-folic acid agents tend to interfere with such growth. Thiersch (*136*) administered 2 mg of aminopterin (an anti-folic acid agent), followed by 3 to 10 subsequent treatments of 1–2 mg at 12-hr intervals to human beings (the number of treatments depending upon the size of the patient and the age of the embryo or fetus), and obtained spontaneous abortions in 10 out of 12 cases.

Nelson *et al.* (*137*), referring to previous work, stated that studies had shown that the addition of a pyridoxine antagonist (desoxypyridoxine) to a pyridoxine-deficient diet resulted in a high incidence of fetal resorptions when normal adult rats were placed on such a diet 10 to 20 days prior to breeding, and that supplementation with pyridoxine on the day of breeding counteracted the adverse effects of the antagonist. They went on to show then that pregnancy in pyridoxine-deficient animals could be maintained to a significant degree by injection of 1 μg of estrone plus 4 mg of progesterone daily, but not by either hormone separately. They stressed that the results indicate an inadequacy of ovarian hormone secretion in pyridoxine-deficient animals.

Goldman (*138*) observed testicular atrophy and liver steatosis in cholesterol-fed hamsters.

Cosla (*139*) states that the action of ions and enzymes is as important in reproduction as that of the hormones, and that reproduction will fail to occur in certain plant forms in the absence of trace amounts of magnesium. Visscher *et al.* (*140*) found that animals maintained on diets containing trace amounts of certain metallic ions (Na, K, Ca, Mg) showed low reproductive performance, and that this condition could be corrected by adding α-tocopherol, or vitamin B_{12}.

Gassner *et al.* (*141*) refer to the work of Mann and co-workers and state that in the rabbit a close relationship exists between endocrine activity of the testis and the rate of fructose elaboration in accessory sex organs.

VIII. *Special Agents*:

Specific Compounds. Prior and Ferguson (*142*) administered the antibactericidal drug nitrofuran (20 per cent in the diet) to rats and obtained a condition of complete aspermia within 1 week. Similar results were obtained with furacin by Friedgood *et al.* (*143, 144*), who observed the effects in man in connection with cancer therapy. Nelson (*145, 146*) administered furadroxyl (1.5 mg/kg in the diet) to rats and obtained complete aspermia within 4 weeks. In all cases spermatogenesis returned to normal or higher levels after termination of treatments.

Lithospermum. Train *et al.* (*147*), in a study of utilization of desert plants of the Southwest, reported that certain American Indians used an infusion made from the desert plant *Lithospermum ruderale* as an oral agent for control of fertility, the women drinking a cup of this concoction once daily during periods when they wished not to conceive. Cranston (*148*) performed a series of experiments on mice and found that a fluid extract, mixed with normal diet, rapidly induced suppression of the estrous cycles in addition to lowering birth incidence in breeding females. Cranston suggested that the active factors derived from the herb act directly on the pituitary gland, suppressing release of gonadotropic hormones.

Suppression of estrous cycles with *Lithospermum* has also been observed by Drasher and Zahl (*149*), Zahl (*150*), Cranston *et al.* (*151, 152*), Plunkett *et al.* (*153*), Noble *et al.* (*154, 155*), Plunkett and Noble (*156*), Zahl and Nowak (*157*), and Weisner and Yudkin (*158*). Zahl observed that, whereas the sex organs go into a state of quiescence and increased fibrosis, removal of *Lithospermum* materials from the diet causes an immediate return to normal estrus and reproduction. No deleterious effects were observed in the pituitary, thyroid, suprarenals, or pancreas, and only passive fibrosis in the ovaries or uteri. Noble *et al.* (*155*) found the gonadotropin of pregnant mare's serum markedly susceptible to *in vitro* inactivation with crude *Lithospermum* extracts. This fact, combined with Zahl's observation that no histological changes are noted in the pituitary, suggests that *Lithospermum* may act by direct neutralization of gonadotropins. Attempts to obtain purified fractions of *Lithospermum* have not been successful.

Oil of Pisum Sativum. Nag (*159*) fed rats on a diet containing *Pisum sativum* for 8 months and obtained no young during this interval; however, when the *P. sativum* component was replaced by *P. arteneum*, litters were obtained.

Sanyal (*160, 161*) has developed an extract from the *P. sativum* which he states has fertility control action.

Sulfhydryl Groups. MacLeod (*162*) presents evidence indicating that —SH groups play an important role in the energy-producing mechanism of sperm, and that the motility and metabolism of human sperm are inhibited *in vitro* by substances which have an affinity for sulfhydryl groups.

Herbs. Historical accounts of the habits and practices of various primitive and remote peoples frequently make reference to concoctions taken orally for fertility control purposes. In a separate communication there is a list of more than 70 herbs used in such concoctions. Although many of these preparations have been dispensed by herb doctors and have been associated in one way or another with sorcery and witchcraft, it is possible that, through scientific studies, some will be found effective. *Lithospermum ruderale*, dealt with above, is an outstanding example of an herb used by primitive groups and later found fully effective by scientific groups.

IX. *Nervous Stimuli*:

Many experimental and clinical observations indi-

cate that emotional states or other nervous stimuli produce changes in the female genital tract. In certain birds and in ferrets, light factors have been found to act by means of nerve pathways to induce pituitary secretion of gonadotropins (*163*), thus accounting for seasonal reproductivity. On the basis of these and other findings, commercially profitable methods of increasing egg-laying in chickens have been found. Of interest is the fact that nulliparous adult rats or mice can be induced to lactate by foster nursing. Studies by Ingelbrecht (*164*) indicate that lactation and anovulation may result from mammary manipulation.

In certain animals pseudopregnancy occurs. In the case of sterile matings or of mechanical stimulation of the uterine horns, corpora lutea persist in the ovary, and the uterine reactions simulate those which occur normally during the early stages of pregnancy, several estrous periods being missed. Anovulatory pseudopregnancy-like conditions accompany normal lactation and induce lactation as described above. In the rabbit, ovulation occurs as a rule only after the stimulus of coitus. Coitus may occasionally induce ovulation in the human female (*165*), and, in human beings, false pregnancy (pseudocyesis) is associated with psychic crises of various kinds (*166*). Friedgood (*167*) states that there is growing opinion that unconscious emotional conflicts constitute one of the etiological factors in sterility and that neuro-psychodynamic factors are of etiologic significance in impotence and amenorrhea as well as sterility.

All these conditions are initiated by nervous stimulation, including stimuli appearing to come from the subconscious mind, and they offer the prospect that reproduction may, under certain conditions, be controlled by nervous stimuli applied at the right time and in the right way.

X. *Rhythm*:

Of interest from the standpoint of fertility control is the rhythmic occurrence of ovulation. In the human female ovulation usually takes place near the middle of the menstrual cycle. Statistically, if coitus is avoided during the period of the ninth through the seventeenth days after the beginning of menstruation, the frequency of conception is reduced. Owing to irregularities in ovulation time in different individuals and also the lack of really satisfactory means of detecting the time of ovulation even in the same individual, however, use of the rhythm method of controlling fertility gives no real assurance of control. If a simple method were available that women could use to determine with certainty when ovulation occurs, the method would become much more reliable; furthermore, the period of avoidance of coitus could be reduced to 2 days or less, since the fertilizable life of the ovum is short (36 hours or less.

The suggested approaches for physiologic control of fertility are brought together here for more specific identification and for additional comment.

1) *Estrogens and Androgens*: These agents can be administered orally or injected into males or females; they prevent pituitary secretion of FSH and thereby prevent follicle growth in the female and spermatogenesis in the male. Minimal doses, the most effective patterns of treatment, and the full significance of side effects have not yet been determined. The view prevails among clinicians that large doses of estrogens or androgens are required to prevent ovulation. Certain animal evidence suggests the possibility of control with dosages within the limits of the physiologic range.

2) *Progesterone*: This agent can be given to females and prevention of ovulation obtained; but, as in the case of estrogens and androgens, minimal doses, the most effective treatment patterns, and the extent of side effects are not known.

3) *Prolactin*: Prolactin, administered orally or injected into females, is believed to result in increase of progesterone output and in inhibition of pituitary secretion of LH, thereby preventing ovulation; detailed information is lacking.

4) *Pregnanediol* (non-estrogenic fraction): This end product of progesterone metabolism is antagonistic to progesterone, and its use prevents decidual growth and might be expected to prevent ovulation or implantation or both; little is known as yet about its practical value for fertility control.

5) *Anti-gonadotropins*: Bodies immune to pituitary gonadotropins can be created to prevent follicular growth and ovulation; requirements for effective control and practical means of supply of agents have not been developed.

6) *Phosphorylated Hesperidin*: This agent is believed to act by preventing dispersion of follicular cells around the ovum, thereby preventing fertilization. Positive fertility control results based on studies in animals and human beings have been reported. Some information about dosages and patterns of treatment is available. If previous findings can be repeated, further developments are needed to reduce the required frequency of medication.

7) *Spermatotoxins*: Bodies immune to the protein materials of sperm from the same or other species have been obtained; both positive and negative results have been obtained with respect to control of fertility by means of spermatotoxins. Validity of the approach remains in question.

8) *Wharton's Jelly*: Positive fertility control results have been obtained in preliminary experiments utilizing crude extracts of Wharton's Jelly as antigens. Confirmation of the results is needed.

9) *Microorganisms*: Evidence indicates that bacteria or yeasts, which sometimes exist unnoticed in the vagina or uterus, are responsible for infertility. Tests are needed to determine whether such organisms can be transmitted from one patient to another without harm, and whether they can be relied upon for fertility control.

10) *Nitrofurans—Furacin and Furadroxyl*: Preliminary experiments indicate that these agents stop

spermatogenesis in the miotic phase. More experiments are needed to determine their practical value.

11) *Lithospermum*: Crude extracts of the desert plant *Lithospermum ruderale* are reported to have been used by Indians of the Southwest as oral contraceptives. Animal experiments confirm the fact that this agent stops ovulation. Additional developments are needed to purify and standardize the active ingredient, and to test for deleterious side effects.

12) *Extracts of Pisum sativum*: Preliminary experiments indicate that substances from the garden pea prevent fertility. Confirmation studies are needed.

13) *Vitamin A Deficiency*: Prolonged gestation and difficult parturition have been shown to result from lack of vitamin A in the diet.

14) *Vitamin E Deficiency*: Successful gestation has been found to depend upon vitamin E.

15) *Vitamin B_{12} Deficiency*: Testicular degeneration has been shown to occur as a result of the absence of vitamin B_{12} from the diet.

16) *Arginine Deficiency*: Amino acid content in sperm is high. Absence of arginine in the diet has been shown to result in formation of ineffective sperm.

17) *Folic Acid Deficiency*: Folic acid is a requirement for successful gestation. Anti-folic acid agents cause a termination of development.

18) *Metallic Ion Deficiency*: Animals maintained on diets lacking in certain metallic substances show low reproductive performances.

19) *Nervous Control*: Certain sensory and psychic stimuli interfere with the reproductive process. No practical methods have been developed for utilizing this type of information.

20) *Rhythm*: If the time of ovulation is known, the opportunity for fertilization can be avoided. No simple means of determining ovulation has as yet been developed.

Twenty leads for physiologic control of fertility have been listed. Other leads could be drawn from the material presented, and still others could be drawn from literature not mentioned here.

In a general way, the various approaches fall into research categories as follows:

1) *Hormone and enzyme research*, involving estrogens, progesterone and related compounds, androgens, anti-hormones, anti-enzymes, and other substances affecting the mechanism of control of fertility; also agents which have a highly specific effect such as the nitrofurans, aminopterin, and phosphorylated hesperidin.

2) *Immunological research*, involving studies of spermatoxins, Wharton's Jelly, and the like.

3) *Symbiotic organism research*, involving bacteria, yeasts, and other organisms which inhabit the reproductive organs and cause temporary infertility.

4) *Fluid physiology research*, involving media of the Fallopian tubes, cervical mucus, and semen.

5) *Dietary research*, involving vitamins, anti-vitamins, substrate materials, metallic ions, and special substances of various kinds.

6) *Neuro-hormone research*, involving psychic and sensory stimuli acting upon the endocrine system.

7) *Rhythm research*, involving the determination of fertile and infertile periods in the menstrual cycle.

The work in relation to nearly all approaches divides naturally into four stages:

1) *Animal studies*: to test the soundness of approaches.

2) *Biochemical development*: to purify and standardize agents and make them available at low cost.

3) *Clinical investigations*: to determine the reliability of methods in human beings, minimal doses, and the most effective patterns of treatment.

4) *Pilot testing*: to determine methods of achieving utilization of fertility control procedures.

Some of the existing leads (phosphorylated hesperidin, progesterone, *Lithospermum*, and aminopterin) are at a point of development where pilot testing becomes a matter requiring consideration; some have been used in human beings for fertility control purposes with varying degrees of success (phosphorylated hesperidin, aminopterin, spermatoxins, Wharton's Jelly); some represent by-products of experiments carried out for other purposes; and some represent preliminary research leads only.

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News and Notes

Tropical Building Design and Construction Symposium

THE symposium, "Scientific Principles and their Application in Tropical Building Design and Construction," held under the auspices of the UNESCO Science Co-operation Office for South Asia (SASCO) and the National Institute of Sciences of India (NISI), was the outcome of the collaboration of these two bodies, with substantial assistance from several technical departments of the Government of India, which furthermore made a generous financial contribution to its fund.

A strong Organizing Committee, which, with various sub-committees was responsible for the details of the arrangements, was appointed with representatives of the Government of India in the Ministries of Housing, Works and Supplies; Natural Resources and Scientific Research; Defense; the Council of Scientific and Industrial Research; and of a number of professional institutions and industrial organizations interested in building, construction, and housing problems. J. L. Sarin, of NISI was the secretary of the committee.

Approximately 150 delegates from India, Burma, Ceylon, and Indonesia, attended the symposium. Foreign consultants invited by UNESCO from England, Holland, and Israel, were present to guide its deliberations, and observers from various United Nations organs and specialized agencies participated in the meetings.

The opening session took place in the auditorium of the National Physical Laboratory of India, New Delhi, December 21, 1952. It was inaugurated by the Prime Minister of India. On this occasion, Shri K. D. Malaviya, Deputy Minister of Natural Resources and Scientific Research, S. L. Hora, president of NISI, and P. C. Young, head of SASCO, also delivered addresses. Messages were delivered by foreign delegates on behalf of their countries, Ceylon, Burma, and Indonesia; and by the representatives of ILO, WHO, and ECAFE. In the afternoon, leading technical papers were read by Indian and foreign experts on subjects covering practically the entire field of the symposium. Afterwards, the delegates were the guests at a reception given jointly by SASCO and NISI.

On subsequent days, the symposium met in five sections dealing with (1) Design and Planning, (2) Materials, (3) Production and Building Practice, (4) Ancillary Services for Sanitation, Comfort, and Public Health, and (5) Research, Testing, Documentation, and Technical Training. Attendance at these section meetings was good (about 150 on the average). The total number of complete papers submitted was 80, of which two-thirds were by experts from within the region itself and one-third from the consultants or other foreign specialists. Over 20 written précis of papers which were not, however, later communicated to the organizers, were also received. As far as possible the papers were mimeographed and distributed beforehand. Thus most of the time at the session was left free for the discussion. One point which became apparent was that scientific workers and engineers in

this region, realizing the great complexity of the housing problems, were alive to the necessity of doing systematic and scientific research to solve them.

The closing session was held on the afternoon of December 24, 1952. The chairmen of sections presented their report of the discussions, summarizing the conclusions that could be drawn from them. These were adopted after some modifications proposed by the members. Individual participants, acting as spokesmen of the members present from their country, then gave in turn their impressions of the symposium, more particularly in the light of their national needs. Similarly, the observers from the various international agencies gave their views, indicating in conclusion the nature of the assistance which their organizations were in a position to offer to the region toward the solution of its housing problems. From these speeches, the appreciation of the participants as a whole in the scientific and technical nature of the symposium was manifest. As one of the leading engineers, speaking on behalf of the Indian delegates, said: "The members had undergone a valuable and indeed stiff refresher course," during the symposium; they were grateful to UNESCO and NISI for having brought them, engineers, architects, builders, town planners, and scientists, all together for the first time, thus enabling them to pool their knowledge and to exchange ideas and experience to their great mutual advantage.

Side by side with, and at the same time as, the symposium, an exhibition on housing was held, which proved very popular, and attracted a large number of visitors. This included a display of building literature and documentation, specially collected for the occasion from all over the world. Its usefulness was appreciated by all, particularly by the participants in the symposium itself.

A number of films were shown which proved to be extremely interesting, dealing with aspects of the building industry and of building research. They included some specially loaned for the purpose by the British Building Research Centre.

A program of social events for delegates and their wives was also arranged, including a reception at Rashtrapati Bhawan (Government House) by Sardar Swaran Singh, Indian Minister of Housing, Works, and Supply, and another on the spacious lawns of the National Physical Laboratory by the DLF Housing and Construction Ltd.

After the conclusion of the symposium on December 24, a number of delegates took part in visits arranged for them to sites of architectural importance in the area, notably to Agra, Fatehpur Sikri, and Chandigarh (the new capital town of Punjab under construction); and in the Karnal district to a representative number of the 4000 houses built of stabilized earth by the local state government several years ago, since when they have stood successfully the test of time.

J. L. SARIN

National Institute of Sciences of India
New Delhi

Scientists in the News

Chester M. Alter, Dean of Boston University's graduate school, has resigned to become Chancellor of the University of Denver.

E. N. Beesley of Eli Lilly and Company has been elected a vice president of Health Information Foundation, New York. **James J. Kerrigan** of Merck and Company and **W. D. Malcolm** of Lederle Laboratories have been appointed to the Foundation's operating and executive committees, respectively.

Karl Hilding Beij, acting chief of the Hydraulics Section of the National Bureau of Standards, has retired after more than 32 years of distinguished service. Known for his work in hydraulics and aeronautic instruments, Mr. Beij holds several patents relating to aircraft sextants, and designed the Bausch and Lomb Sextant used before and during World War II.

Howard L. Bender, Assistant Director of the Research and Development Department, Bakelite Company, received the John Wesley Hyatt Award of the Society of the Plastics Industry. Dr. Bender was honored during the convention cruise of the Society on the *Queen of Bermuda,* in recognition of his lifetime of research in the molecular structure of phenolic resin.

Charles S. Cameron has been elected president of the Commission on Cancer Control of the International Union Against Cancer. Dr. Cameron, medical and scientific director of the American Cancer Society, will sail for Europe in June to discuss plans for worldwide control of cancer.

Gordon B. Carson, former engineering faculty member at Case Institute of Technology, has been named dean of the College of Engineering at Ohio State University, effective July 1. Mr. Carson will succeed the late **Charles E. MacQuigg.**

Edwin H. Dahlgren, Fish and Wildlife Service fishery biologist, has left for Djakarta, Indonesia, on a two-year assignment to assist with expansion of the cooperative fisheries development program now under way. **Willis Horton Rich,** also of the Fish and Wildlife Service, is recently back from a six weeks' assignment in Indonesia, and has recommended the continuance of the cooperative program.

August H. Doermann of the Oak Ridge National Laboratory has been appointed Associate Professor of Biology at the Biological Laboratories of the University of Rochester, where he will sponsor training and research in virology and microbial genetics.

Johannes Frandsen, Director of the National Health Services of Denmark, has been awarded the Leon Bernard Foundation prize by the World Health Assembly, meeting at Geneva, Switzerland. Dr. Frandsen was honored for contributions and practical achievements in social medicine.

John F. Fulton, Sterling Professor of the History of Medicine at Yale University, has been elected a Fellow of the Royal College of Physicians, London.

J. E. Hedrick of Cornell University's chemical engineering faculty has been appointed Assistant Dean of the College of Engineering at Cornell.

T. Howard James, Research Associate at Kodak Research Laboratories, has been awarded a Davanne Medal by the French Photographic Society. G. I. P. Levenson, Harrow, England, and Mlle. A. M. Venet, Vincennes, France, Kodak research workers overseas, also received Davanne medals.

Donald H. Loughridge, assistant director for reactor development for the Atomic Energy Commission, has been named dean of Northwestern University's Technological Institute, effective July 1.

Manuel Nuno has been appointed the first technical representative of Fisher Scientific Company in Mexico. Mr. Nuno will assist chemists, metallurgists and pathologists in Mexico's growing industrial, research, clinical, and university laboratories.

C. H. B. Priestley, Officer-in-Charge of the Commonwealth Scientific and Industrial Research Organization, Section of Meteorological Physics, Highett, Victoria, Australia, has been awarded the degree of Doctor of Science of the University of Cambridge for his published research on meteorology.

David J. Rogers, Assistant Professor of Biology, Allegheny College, Meadville, Pa., will do field work in Jamaica and Costa Rica this summer, in connection with his study of the taxonomy of the varieties of *Manihot utilissima.*

G. Milton Shy has been appointed Chief of Clinical Research of the National Institute of Neurological Diseases and Blindness, where he will be responsible for clinical research in the neurological and sensory disorders. The Institute has been allocated beds and laboratories in the Clinical Center, the new research facility at Bethesda, Md.

Sir Arthur Smout has been elected a fellow of the Institute of Metals, London. Sir Arthur has been a member of the Institute since 1917, and has served as member of council, vice president and president.

Arthur E. Teeri will succeed **Thomas G. Phillips** as Chairman of the Department of Agricultural and Biological Chemistry, University of New Hampshire, effective July 1. Dr. Phillips will continue in the department.

Charles L. Thomas, formerly manager of the Research Laboratory of the Sun Oil Company, Norwood, Pa., has been appointed associate director of the department in charge of line activities at Marcus Hook, where Sun is currently building laboratories.

F. M. Van Tuyl will retire as head of the Department of Geology at Colorado School of Mines, effective this summer. He will be succeeded by **L. W. LeRoy,** Professor of Geology, and a member of the Mines faculty since 1942.

W. J. Van Wagtendonk has received a grant from Eli Lilly and Company to investigate the steroid requirements of Paramecium aurelia in axenic medium and the interaction of steroids. Dr. Van Wagtendonk is a member of the Department of Zoology at Indiana University.

Walter O. Walker, Professor of Chemistry and Director of Industrial Chemical Research, University of Miami, Coral Gables, Fla., has been appointed Dean of the Division of Research and Industry at Miami. His new duties will include coordinaton of all research studies at the university.

Education

Dartmouth College has acquired an extensive library on the polar regions, assembled over thirty years by Vilhjalmur Stefansson, polar explorer and Arctic consultant to the college museum. Funds to buy the collection were given by Albert Bradley, executive vice president of General Motors and a Dartmouth alumnus.

A month's course in Medical Mycology will be offered at **Duke University School of Medicine,** Durham, N. C., in July, under the direction of Norman F. Conant. Meeting six days a week, the course is designed to insure a working knowledge of the human pathogenic fungi within the time allotted. Applications will be considered in the order received, and information is available from Dr. Conant at Duke.

The fifth **"March of Medicine"** television program, sponsored by the American Medical Association and Smith, Kline & French Laboratories, will be broadcast from the AMA meeting in New York, June 4. The program will honor the profession of pharmacy, contrasting the apothecary shop of 160 years ago with the prescription pharmacy of today.

Dedication activities for the new Cancer Research Laboratories at **Ohio State University** included a Cancer Symposium and an exhibit of the research being conducted. The dedication ceremony for the four-story structure, made possible by grants from Ohio, the U. S. Public Health Service, and the Charles Kettering Foundation, was held May 9.

The Kresge Science Library, at **Wayne University,** was formally dedicated May 14. Stack space in the new building will accommodate the more than 50,000 science volumes and periodicals making up the Kresge-Hooker collection, as well as future accessions. Study space will be provided for students, faculty, industrial research workers, visiting scholars, and advanced students. Harold C. Urey delivered the dedication address on May 15, entitled "Science and Society."

Grants and Fellowships

The **California Institute of Technology** has received a grant of $10,000 to support the work of the Committee for Aid to War-Stricken Libraries. The Committee, headed by Fritz Zwicky, Professor of Astrophysics, was formulated to send unclassified scientific material to needy libraries abroad. The foundation grant will be used mainly for shipping charges, since the literature is all donated.

The **University of Connecticut** has received a Frederick Gardner Cottrell grant of $4962.50 from the Research Corporation for low temperature physics research. Charles A. Reynolds, low temperature physicist, will direct the supported research entitled "Experimental Investigations of the Hydrodynamics of Liquid Helium II—Heat Transfer in Helium II."

The **Fund for the Advancement of Education** has granted 252 fellowships to college faculty members in the U.S., Hawaii, and Puerto Rico, for the academic year 1953–54. These grants, aggregating more than $1,400,000, are designed primarily to enable the recipients to become better qualified to teach in their respective fields, which include the humanities, the social sciences, and the natural sciences.

The **University of Michigan** has received a grant of $1,000,000 from the Ford Motor Company Fund for construction on the Ann Arbor campus of a nuclear reactor to be used in nonmilitary research. The new reactor will be housed in the Phoenix Memorial Laboratory, for which ground will be broken this year.

A fellowship in wood chemistry has been established by the Weyerhaeuser Timber Foundation at **Northwestern University.** Northwestern is the sixth educational institution to be granted WTF fellowships.

In the Laboratories

Production of gamma globulin has begun in **Armour & Company's** new plant at Bradley, Ill., financed by the National Foundation for Infantile Paralysis. Armour will turn over the product to the allocating authority for distribution from the national pool

A new **Atomic Energy Commission** laboratory located in Winchester, Mass., is in full operation. The primary objective of the laboratory, operated by the American Cyanamid Company under contract to the Raw Materials Division of the AEC, is the development and improvement of processes for the recovery of uranium from its ores. All phases of mineral dressing will be studied, and one of its functions will be to undertake the task of developing methods for recovery of uranium from low-grade uranium-bearing materials.

Edison Research Laboratory scientists have developed a heat-sensitive cable that will stand up under 2000° F and signal an alarm if touched by flame at any point. Announcement of the completion of several years of research was made by Henry G. Riter, III, President, at the opening of a new $500,000 research laboratory at West Orange. Robert H. Postal of the Edison research staff, in conjunction with F. G. Kelly, was credited with discovering the thermister material from which the cable is constructed.

The **Harvard School of Dental Medicine** has opened a new addition to its building that will almost double the available space for research seeking the causes of dental disease. This research ranges from submicroscopic analysis of the structure of the teeth to biochemical studies involving endocrine and nutritional factors in the growth and development of the face and jaws.

The **Merck Institute for Therapeutic Research** has opened a new center for research. Nearly 400 scientists, educators, government officials, and business leaders attended the dedication ceremonies. Alan Gregg, Vice President of the Rockefeller Foundation, and Alfred E. Driscoll, Governor of New Jersey, were the principal speakers.

Four staff engineers at **Monsanto Chemical Company** have been appointed assistant directors in the General Development Department. Promoted to the new posts were: Robert H. Kittner, C. Rogers McCullough, David S. Weddell, and Robert York, Jr.

A new plant of the **Union Carbide and Carbon Corporation** has been opened at Institute, West Virginia. This is the first commercial plant in the world to produce chemicals directly from coal.

Meetings and Elections

The **American Academy of Arts and Sciences,** at its Annual Meeting in Boston, elected 97 new Fellows and five Foreign Honorary Members. Elected as officers for the coming year were: president, Edwin H. Land of Polaroid Corporation; vice president for mathematical and physical sciences, Francis Birch, Harvard University; vice president for biological sciences, James M. Faulkner, Boston University School of Medicine; vice president for social arts and sciences, Edwin D. Canham of the Christian Science Monitor; vice president for humanities, John E. Burchard, MIT; secretary, William C. Greene, Harvard; treasurer, Horace S. Ford, MIT; and librarian and editor, Taylor Starck of Harvard.

D. S. Gilmore of the Upjohn Company, Kalamazoo, Mich., was re-elected president of the **American Drug Manufacturers Association** at the annual meeting at Boca Raton, Fla., April 15. Elected vice presidents were: W. L. Dempsey, of Sharp & Dohme; J. H. F. Dunning, of Hynson, Westcott and Dunning; T. G. Klumpp, of Winthrop-Stearns; and E. H. Volwiler, of Abbott Laboratories. M. C. Eaton, of the Norwich Pharmacal Company and Eaton Laboratories, was elected treasurer.

More than 3000 leading biologists from the Western Hemisphere will present some 2000 papers on their scientific findings and will conduct eight symposia on major biological problems at the annual convention of the **American Institute of Biological Sciences** at the University of Wisconsin, Sept. 6–10.

New officers of the **American Psychosomatic Society** include: president, George L. Engle; president-elect, Lawrence S. Kubie; and secretary-treasurer, Theodore Lidz. Robert A. Cleghorn, Jacob E. Finesinger, and Jurgen Ruesch were elected to council positions.

A conference was held at **Amherst College** May 4–6 to discuss the status of physics research in colleges not offering graduate work. The conference was sponsored jointly by the National Science Foundation and Amherst College, and Theodore Soller of Amherst was chairman. There were 25 in attendance, representing colleges of various types in all regions of the country. The conferees agreed that doing research in colleges was helpful in carrying out the educational functions of the college. It was recommended that the Federal Government consider special research grants or contracts in colleges, directly for research and indirectly to improve the training and education of physics students. In addition to Dr. Soller, the committee included: W. C. Michels, Bryn Mawr College; K. S. Van Dyke, Wesleyan University (Conn.); Mildred Allen, Mt. Holyoke; C. A. Fowler, Pomona College; R. R. Palmer, Beloit College, and J. H. McMillen, NSF.

A new organization, the **Association of University Anesthetists,** has been formed to advance the art and science of anesthesia by encouraging original investigations, by developing methods of teaching, and by such free and informal interchange of ideas as a limited membership and common aims make possible. The organizing committee included physician anesthetists from Columbia, Harvard, Minnesota, Pennsylvania, Tufts, Vanderbilt, and Wisconsin. Additional anesthetists have been elected from these universities, and from the following medical schools: Albany, Boston, Cornell, Duke, Georgia, Johns Hopkins, New York, New York State, Oregon, Rochester, Texas, Tulane, Washington, Wayne, and Yale.

The Northeastern Section of the **Botanical Society of America** will hold its seventh annual summer excursion in the Adirondack Mountain area of New York June 16–19. Headquarters will be at Champlain College in Plattsburg. Information may be obtained from Dr. E. C. Ogden, New York State Museum, Albany.

The Safety Awards Committee of the **Joseph A. Holmes Safety Association** has approved 527 awards to individuals and companies for the promotion of safety in the mining, mineral, extractive, and related industries. The Hero Award Committee also approved 9 Medals of Honor and 2 Certificates of Honor for individuals who were instrumental in saving life or avoiding injury.

The **National Advisory Councils,** nonfederal groups that advise the Public Health Service, will meet twice a year instead of three times. The meetings will be held in June and January at the National Institutes of Health, Bethesda, Md. One of the principal functions of the Councils is to advise the Surgeon General with regard to research, teaching, and training grants. The National Institutes of Health Study Sections, which provide the Councils with advice on grant applications, will also meet twice a year, in April and November. Applications received by August 15 will be considered at Council meetings in January, 1954, and those received by January 15 will be considered in June.

Three new members have been appointed to the **National Research Council of Canada,** and three retiring members have been reappointed. New members include R. F. Farquharson, University of Toronto, and E. G. D. Murray and David L. Thomson, McGill University. The Council members who have been reappointed are C. W. Argue, University of New Brunswick, A. G. McCalla, University of Alberta, and G. M. Shrum, University of British Columbia.

The next scheduled meetings of the **Scientific Advisory Committees** to the Division of Biological and Medical Sciences of the National Science Foundation will be held in late autumn, 1953. To be considered at these meetings proposals for research support must be received by the Foundation prior to Oct. 1, 1953. It is anticipated that evaluation of proposals will be completed within two months after the closing date. The Foundation sponsors basic research in the biological and medical sciences in the broad fields of molecular, genetic, developmental, regulatory, systematic, and environmental biology, and in experimental psychology.

The **Summer Seminar in Statistics** will meet at the University of Connecticut, Aug. 10–28. The first week will be concerned with statistical method in physics, the second with statistics in biometry and medicine, the third with the ASA Handbook and with performance and reliability of complex mechanical assemblies. The sessions may be attended for a day, a week, or other period. Information may be obtained from Prof. Geoffrey Beall, Statistical Laboratory, University of Connecticut, Storrs, Conn.

The sixth annual **Symposium on Crystal Chemistry as Applied to Ceramics** will be held at the Massachusetts Institute of Technology on June 18. William D. Kingery, Assistant Professor of Ceramics at MIT, is in charge of arrangements.

A new **Tobacco Research Advisory Committee** has been appointed by the Board of Control of the Connecticut Agricultural Experiment Station. Made up of prominent tobacco growers, representing all phases of the industry, the committee was formed to consult with the Station on policy to be followed on future research. Meeting with the committee were board

members John Lyman, vice president, James G. Horsfall, director, and William L. Slate, the Station's director emeritus and acting head of the Tobacco Laboratory at Windsor.

Officers of the **West Viriginia Academy of Science** for 1953–54, elected at the annual meeting held at Morris Harvey College, Charleston, are: president, E. E. Myers; vice president, Robert C. Colwell; secretary, J. T. Handlan, Jr.; treasurer, H. D. Bennett.

At the **World Health Organization** meeting in Geneva in May, Murchad Khater, Minister of Health of Syria, was elected president. Vice presidents elected were Saiful Anwar of Indonesia, Roberto Caceres Bustamente of El Salvador, and Melville D. Mackenzie of Britain. The Director-General, Brock Chisholm of Canada, will be succeeded by M. G. Candau of Brazil. Dr. Chisholm's five-year term expires on July 21.

Miscellaneous

The **American Museum of Natural History** has opened Brontosaur Hall, a newly designed exhibition of life on earth more than two hundred million years ago. The hall, which contains the world's largest collection of early fossil amphibians and reptiles, was under reconstruction for more than a year. Scientists, artists, and craftsmen combined their efforts to create a dramatic setting in which to tell the story of life millions of years before the earliest man.

Consultants Bureau, 152 W. 42nd St., New York, will publish separate tables of contents to each issue of the English translation of the following Russian chemical journals: The *Journal of Analytical Chemistry*; the *Journal of Applied Chemistry*; the *Journal of General Chemistry*; *the Bulletin of the Academy of Sciences of the U.S.S.R, Division of Chemical Science*; and *Colloid Journal.* The tables of contents will be mailed without charge if requested on an official letterhead. Any paper listed may be purchased for $7.50.

John Behnke, Associate Administrative Secretary, served as AAAS representative at the dedication of the **Ford Motor Company Archives** at Fair Lane, the late Henry Ford's home in Dearborn, Mich. The ceremonies were part of the celebration of the Golden Anniversary of the Ford Motor Company. A staff of researchers are sorting and cataloging some 5,000,000 letters and company papers and 25,000 photographs. A unique feature is the recording of interviews with those who have had some part in the Company's development or in the lives of Henry and Clara Ford. Of the 300 to 500 people to be questioned, some 225 have already recounted their recollections, and the total will amount to some 13,500,000 words. Recorded on tape, transcribed, and then carefully edited, each participant's material forms a bound volume in its chronological niche in the reference room of the Archives. In addition, the Archives library includes 7500 books and 187 volumes of newspaper clippings. The visitors were also shown the Scientific Laboratory where, during the first year of its operation, over 140 scientists and engineers have been assembled to conduct basic and applied research.

The **New York Zoological Society** has appointed McGraw-Hill's Text-Film Department as the distributor of its current and future films. Four 10-minute films dealing with mammals, birds, and fish in the Bronx Zoo and the New York Aquarium are now available in black-and-white and color. Ten other films on reptiles, African mammals, baby animals, and great zoological rarities are planned by the Society for distribution in the next two years.

The 200th anniversary of the publication of ***Species Plantarum,*** by Carl Linnaeus, or Carl von Linné, was observed May 19 by an international group of botanists in Cambridge, Mass. The plan for the jubilee originated in the Netherlands, where Linnaeus' system for the classification of plants was originally accepted, and where the International Bureau for Plant Taxonomy and Nomenclature is now publishing a special issue of its magazine, *Taxon.*

The **U.S. Atomic Energy Commission** has awarded a total of 37 unclassified physical research contracts with universities and private research institutions during this year. The contracts, which generally were for a term of one year, were let as part of the AEC's policy of fostering private research to encourage maximum scientific progress in fields related to atomic energy. All the contracts are for basic, rather than applied, research. Contract proposals are reviewed by scientists, and participating institutions assist in defraying the costs of research when it is of mutual interest.

Seven employees and two work units of the **U.S. Department of Agriculture** have received Distinguished Service Awards, 105 employees and 13 work units have received Superior Service Awards, and 46 workers were given recognition for 40 years or more of service. The Department's highest honor, the Distinguished Service Award, will go to Fred C. Bishopp, Bureau of Entomology and Plant Quarantine, Washington, D. C.; Sterling B. Hendricks, Bureau of Plant Industry, Soils and Agricultural Engineering, Beltsville, Md.; Allene R. Jeanes, Bureau of Agricultural and Industrial Chemistry, Peoria, Ill.; Henry A. Jones, Bureau of Plant Industry, Soils and Agricultural Engineering; Joseph M. Mehl, Commodity Exchange Authority, Washington, D. C.; Ernest R. Sasscer, Bureau of Entomology and Plant Quarantine; and R. W. Trullinger, Office of Experiment Stations, Washington, D. C. The two work units receiving the highest honor were the Animal Fat Oxidation Unit, Bureau of Agricultural and Industrial Chemistry, Wyndmoor, Pa., and the Project on the Action of Diisopropyl Fluorophosphate on Esterolytic Enzymes, Bureau of Agricultural and Industrial Chemistry, Albany, Calif.

Technical Papers

Effect of Gamma Irradiation on the Ascorbic Acid Content of Green Plants[1]

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During the summer of 1952 a preliminary investigation of the effect of gamma irradiation on the ascorbic acid content of plants was undertaken. As it is, at this time, impossible for the writer to continue with this work the results of these experiments are presented now.

The effect of continuous irradiation on ascorbic acid content was studied by growing the plants near a source of constant gamma rays. The plants were irradiated continuously, except for short periods of time during the day when it was necessary to enter the gamma field to collect material. Snapdragon plants, varieties rose queen and afterglow growing in pots, were placed 1.3 meters from a 300-curie Co^{60} source. The gamma irradiation at this distance as measured by victoreen r-meter cobalt chambers was found to be approximately 5000 r/day. The control plants received no gamma irradiation. Total ascorbic acid was determined periodically by the method of Roe and Oesterling (*1*). The effect of chronic gamma irradiation on the ascorbic acid level in these plants is shown in Table 1.

TABLE 1

EFFECT OF CHRONIC GAMMA IRRADIATION ON THE ASCORBIC ACID CONTENT OF SNAPDRAGON PLANTS

No. of days in gamma field	Ascorbic acid level in irradiated plants expressed as percentage increase over controls	
	var. rose queen	var. afterglow
2	+ 4.5	−13.8
3	+ 5.7	+10.7
5	+24.5	+41.1
7	+12.4	+47.4
9	+69.4	+51.4

As can be noted from the data there was a rise in ascorbic acid content of the plants with time for a period after the start of irradiation. This rise in ascorbate was noted before there was any visible damage to the plants. The plants did show radiation damage after a longer period of time. A rise in ascorbic acid content was also noted after an acute dosage of x-rays. The relation of x-ray dosage to increase in ascorbic acid content is given in Table 2. In this experiment Biloxi soybean plants were exposed to various dosages of x-rays which were administered at the rate of 1000 r/min. The x-ray machine was operated at 250 kv and 30 ma, with a filter of 1 mm of aluminum. After irradiation the exposed plants were placed in the greenhouse with the control plants.

TABLE 2

EFFECT OF VARIOUS DOSAGES OF X-RAYS ON THE ASCORBIC ACID CONTENT OF SOYBEAN PLANTS

No. of days after irradiation	Ascorbic acid content in irradiated plants expressed as percentage increase over controls		
	1000 r	4000 r	16000 r
2	−10.1	−10.1	− 4.1
3	− 4.5	+19.5	+ 9.1
5	+ 8.3	+18.6	+33.8
10	+ 9.5	+12.9	+28.4

From these and other preliminary experiments it would appear as though the immediate effect of irradiation is a drop in the ascorbate level of the plants. This is followed a few days later by a rise in the ascorbate level, followed some time later by a second decrease in ascorbic acid content. The cause of these increases in ascorbate upon irradiation has not been further investigated. The increase might possibly be due to a decrease in activity of enzymes bringing about the oxidation of ascorbic acid. Weber and Gordon (*2*) were able to show a significant increase in indoleacetaldehyde following x-irradiation and at the same time a decrease in the ability of an enzyme to convert indoleacetaldehyde to indoleacetic acid.

Ascorbic acid is one of the naturally occurring compounds in biological systems that appears to offer some protection against irradiation. Gordon and Weber (*3*) showed that ascorbic acid protected solutions of indoleacetic acid from irradiation. Giri (*4*) showed that isolated enzyme systems were protected by ascorbic acid, and Caffaratti (*5*) was able to show that injection of ascorbic acid into the blood stream of rats protected these animals from whole body irradiation. However, the rise in ascorbic acid content following irradiation of plants as noted in these experiments did not further protect these plants against irradiation damage. An interesting phenomenon noted during the course of these experiments, however, was the apparent correlation between the initial ascorbic acid content and the relative resistance of a plant to irradiation. This was especially noticeable in that part of the work where plants were grown under constant gamma irradiation (*6*). Table 3 shows the relative resistance of a plant to irradiation and the normal ascorbic acid content of that plant.

Table 3 suggests that there may be some correlation between the normal ascorbic acid content of a plant and the sensitivity of that plant to irradiation. Many more species of plants should be examined, however,

[1] This work was carried out at Brookhaven National Laboratory, Upton, L. I., N. Y., while the author was research collaborator.

TABLE 3

ASCORBIC ACID CONTENT AND THE RELATIVE RESISTANCE TO IRRADIATION
(In mg/100 g fresh wt)

Species	Resistant	Moderately resistant	Low resistance
Cabbage	200–300		
Gladiolus	300–400		
Soybean		120–150	
Snapdragon		100–120	
Cosmos sulfureus			90–100
Nicotiana rustica			50– 60
Xanthium spp.			70–100
Hyoscyamus niger			30– 40

before a definite conclusion can be safely drawn. This ability to resist irradiation depends on the plant's normal ascorbic acid content and not on the increase in ascorbate upon irradiation. From these experiments it appears that ascorbic acid may offer a protecting action against irradiation in plants.

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The Ultraviolet Microscopy of the Living Cell's Response to Lethal X-Radiation[1]

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The development of the Polaroid color translating ultraviolet microscope by Land and co-workers (*1*) has brought to biology and medicine a tool capable of following the nucleoprotein changes in living cells subjected to lethal doses of x-radiation. This paper presents the data obtained when tissue cultures of Walker rat carcinoma 256 cells are given a lethal dose of x-radiation and then photographed with the Polaroid color translating ultraviolet microscope for intervals up to 120 hr.[3]

The technical aspects of the Polaroid color translating ultraviolet microscope have been published elsewhere and will not be discussed here (*1–3*). Such data as those given in the following paragraph, however, are pertinent to the experiments reported.

U-V source: High-pressure AH-6 mercury are operated at 600 volts

Wavelengths: 281 mμ, blue filter; 261 mμ, green filter; 250 mμ, red filter

Band-width at half height: 5.3 mμ

Objective: Polaroid-Grey No. V, N. A. 0.72

Condenser: Polaroid-Grey No. V, N. A. 0.72

Diameter of specimen area illuminated: 75 μ

Original magnification to film: 210×

Film type: Kodak Spectrum Analysis #1

Rapidly processed with D-8 developer diluted 2 : 1, at 90° F for 7 seconds

Specular gamma: 1.70

All photographs reported in this experiment gave a background density of approximately 2.20 density units.

All x-radiation was given by a General Electric Maximar therapy unit, 200 kv, 10 ma, inherent filtration 3 mm aluminum, target distance 20 cm.

The tissue culture preparations were made from a suspension of Walker rat carcinoma 256 cells in a nutrient medium composed of 10% embryo extract, 50% human ascitic fluid from a cirrhotic patient, and 40% Hank's balanced salt solution. The suspension was made by excising small pieces of tumor from subcutaneous transplants, and then grinding the fragments lightly with several applicator sticks while they were suspended in medium. One drop of this suspension was then placed on half of a Vycor cover slip, the other half of the cover slip was placed on top, and the excess fluid was removed from the edges. The two halves of the Vycor cover slips were then placed in roller bottle flasks as flying cover slips, with sufficient medium added just to cover them. In this type preparation the surface tension of the cell suspension is sufficient to prevent the cover slips from separating, while medium is permitted to diffuse slowly between. In this fashion the cells maintain a continuous population which covers the area between the cover slips. One-half of the medium was renewed every 3 days. The Slonaker rats in which the tumor was carried subcutaneously were treated with penicillin, and penicillin was added to all cultures. The cell suspensions were made from tumors which were from 10 to 15 days old. All flasks were kept in the incubator at 37.5° C.

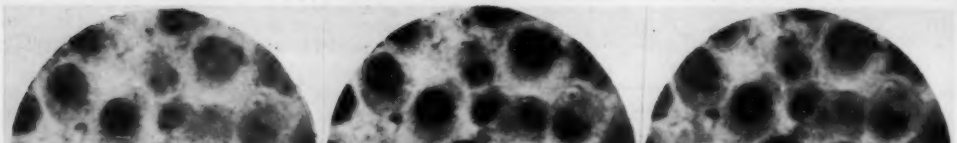
It was determined that approximately 90% of the cells were carcinoma cells by means of supravital stains with Janus green and neutral red, as well as such fixed stains as Wright's and Giemsa's. The remainder of the cells were macrophages.

In all cases the tumor was cultured the day previous to x-radiation, and control cultures made and carried under identical circumstances. The day of photography the cultures were washed with balanced salt solution by substituting it for the medium for 30 min. The double cover slips were then mounted on

[1] This work was done under U. S. Atomic Energy Commission Contract AT(30-1)-901 with the New England Deaconess Hospital.

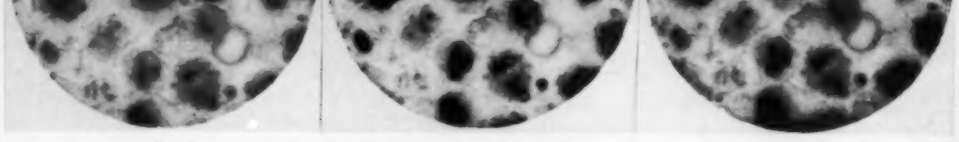
[2] We wish to acknowledge gratefully the technical assistance of Mrs. Staples, Miss Swaffield, Mr. Burns, and Miss Crozier; and to thank E. H. Land, E. R. Blout, and R. J. Barrnett for their advice and encouragement.

[3] The ultraviolet photographs were taken on the Polaroid color translating ultraviolet microscope in the Research Division of the Polaroid Corporation, Cambridge, Mass.



281 A 261 A 250 A

FIG. 1. Untreated Walker rat carcinoma cells.



250 A 261 A 281 A

FIG. 2. Walker rat carcinoma cells 72 hr after 60,000 r.

Vycor slides and sealed with a paraffin petroleum jelly mixture. The photographs were thus of living cells suspended in balanced salt. Except during the process of photography, the preparations were kept in the incubator. The ultraviolet absorption densities of the preparations did not change during the 6-hr period in which the cells were mounted on the Vycor slides.

All radiated cultures were given from 47,000 to 60,000 r. This dose was determined as an approximately lethal dose for these cells under these conditions by two means. (1) This is three times the dose necessary to kill the tumor in the rat. (2) Previous cultures were set up and irradiated under similar conditions from 500 to 100,000 r; and 47,000 to 60,000 r determined as the optimum minimal lethal dose. Sixty thousand roentgens is sufficient to cause disappearance of 98% of the cultured cells within 10 days.

The fields to be photographed were selected at random and a minimum of four fields were photographed on each preparation reported. These fields were always in different quadrants of the slide. Each field was photographed six times in a space of no more than 5 min. In no case were cells exposed to ultraviolet light rephotographed at a later interval.

Irradiated preparations and their corresponding controls were photographed at the following time intervals, beginning with 0 time as the time of the end of irradiation: 30 min, 3 hr, 6 hr, 24 hr, 48 hr, 72 hr, and 120 hr.

In all, a total of 160 fields were photographed in 36 preparations.

Figure 1 is a photograph of a typical field in a control preparation. In all the viable control preparations through 120 hr, cells identical with these were present in all the fields photographed. Similar cells were likewise present in every field of every x-radiated preparation up to 48 hr. Indeed up to this point the controls and the irradiated cultures could not be distinguished. Figure 2 is a typical photograph of a field from an x-radiated culture at the end of 72 hr. This photograph is indistinguishable from all other fields photographed in the x-radiated preparations at 48 hr, 72 hr, and 120 hr—with only one exception. This exception was one cell in one field of one 48-hr preparation which showed an absorption density approximately halfway between Figs. 1 and 2.

It is of some interest to note that the control and irradiated cultures could not be distinguished at any time with a conventional light microscope.

From the two photographs one sees at once the striking loss of absorption in ultraviolet light typical of all the cells in the x-radiated preparations examined from 48 hr through 120 hr. This loss of absorption is present in both the cytoplasm and the nucleus, and the clearly defined structures, which absorb so beautifully in the normal cell, are virtually completely absent in the second figure. Together with this change, one gains the impression here—as in the other photographs—that the nuclei of the irradiated cells are swollen. No attempt was made to define in more precise terms this impression, as sufficient data and technical methods are not available to establish this point.

It should be pointed out here that if one photographs dying control material a picture similar to Fig. 2 is obtained—indicating that at these wavelengths the ultraviolet absorption picture of the process of cell death is the same in radiation cell death and cell death due to other factors.

These photographs are reproduced in black and white; when color translated, the black areas appear green, with some gentle shading of yellow and red in the cytoplasm. Clearly visible in color are the cell borders, the cytoplasm, the nuclear membranes, nucleoli, and chromatin. As shown by Caspersson, intense absorption of ultraviolet light at these wavelengths is characteristic of nucleoproteins, both RNA and DNA, and in fact represents in the main absorption by the purine and pyrimidine components of the nucleic acids (*4*).

From these data we are able to say that the ultraviolet light absorbing cell structures in these preparations do not change from normal as determined by the Polaroid color translating ultraviolet microscope until 48 hr after 60,000 r of x-radiation. From 48 hr through 120 hr they undergo a profound change.

This profound change—quantitatively and qualitatively the same from 48 hr on—is reflected in the striking contrast between the photographs in Figs. 1 and 2. The almost complete loss of all absorption in both the cytoplasm and the nucleus, together with the impression of nuclear swelling, is indeed striking. Its interpretation is difficult. Three possible explanations may be offered. We shall discuss them in the order which we consider the most likely.

1) This change may represent an absolute loss of both RNA and DNA amounting to almost complete absence. Nucleoproteins are known to be affected by x-radiation both *in vivo* and *in vitro*, and in dying cells loss of nucleoproteins seems inevitable (*5, 6, 7*).

2) This change might conceivably represent an alteration in the physical state of the nucleoproteins with reference to the more liquid portions of the cell, thus producing an ultraviolet absorption effect simulating loss of nucleoproteins.

3) The change may be accounted for by assuming that the purine and pyrimidine rings—in reality the absorbing structures—have been so changed by the x-radiation that they no longer give their characteristic absorption.

In order to define better the underlying mechanisms of this nucleoprotein change, similarly prepared control and irradiated cultures were studied histochemically at the same postirradiation intervals. No postirradiation change was observed in the acid phosphatase by Glick's (*8*) modification of Gomori's method, in the nonspecific esterase by the method of Barrnett and Seligman (*9*), in the lipid by Sudan Black B staining, or in the protein bound sulfhydryl by the method of Barrnett and Seligman (*10*).

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The Immunochemical Heterogeneity of Human Plasma β-Lipoprotein[1]

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From the protein fractions obtained by the partition of human plasma in ethanol-water mixtures at low temperatures (*1–3*), solutions of β-lipoprotein were isolated and purified in the preparative ultracentrifuge (*4, 5*). Gofman *et al.* (*6*) have reported that human serum lipoproteins show considerable heterogeneity with respect to flotation rates in the ultracentrifuge in a sodium chloride solution of density 1.06. Oncley *et al.* (*7*), on centrifuging relatively concentrated β-lipoprotein solutions for about 18 hr in a glycine-sodium chloride medium of density 1.3, separated three β-lipoproteins of different flotation rates. In an attempt to gain greater understanding of the relationships between lipoprotein metabolism and certain aspects of normal and pathologic human physiology, several investigations have been conducted in this laboratory on the metabolism of human β-lipoprotein. This report presents evidence that the plasma β-lipoprotein fraction is composed of a number of lipoproteins differing markedly in their immunochemical characteristics.

Rabbit antiserum vs human plasma β-lipoprotein

[1] This work was supported by a grant (No. RG-346) from the National Institutes of Health, USPHS.

[2] This work was completed under tenure of a Postdoctorate Research Fellowship, National Institutes of Health, USPHS.

[3] Indebtedness to John L. Oncley and F. R. N. Gurd of the Department of Physical Chemistry, Harvard Medical School, for the preparations of β-lipoprotein used in this study is gratefully acknowledged.

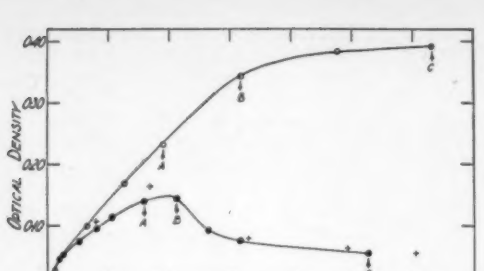

FIG. 1. Precipitation curves obtained by reacting rabbit antiserum vs human plasma β-lipoprotein with preparations of β-lipoprotein obtained from two different pools of human plasma. Arrows: supernatants of these reaction mixtures tested as in Table 1. ○: preparation BS0; ●: preparation BS1.

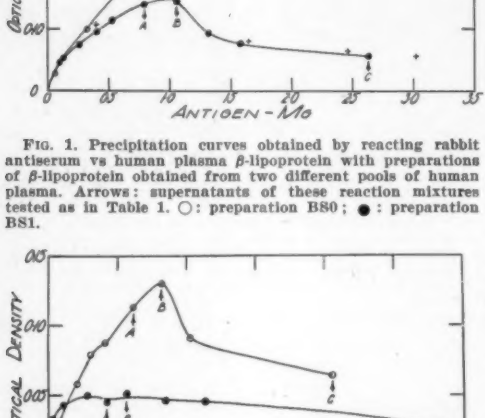

FIG. 2. Precipitation curves obtained by reacting rabbit antiserum vs human plasma β-lipoprotein with preparation BS3 (○) and the lipid-poor fraction, preparation G3 (●), separated during the purification of BS3. Arrows: supernatants of these reaction mixtures tested as in Table 1.

was obtained by using a freshly purified preparation of β-lipoprotein, BSX, separated from pooled plasma by the method of Oncley *et al.* (*5*). The lipoprotein was dissolved in 0.15 *M* NaCl, and this solution was given to rabbits subcutaneously at 10-day intervals, 25 mg/kilo body weight/injection for 4 injections. The first injection was administered within a week of final purification of the lipoprotein in the ultracentrifuge; the solution was kept at 0° to 2° C at all times between injections. Rabbit antisera vs human serum γ-globulin, preparation L413-II-1, and crystallized human serum albumin, preparation Decanol 10 (*8*), were obtained by employing aluminum hydroxide-adsorbed antigens (*9*); rabbits were injected subcutaneously at 7–10-day intervals, 25 mg antigen/kilo body weight/injection for 5 injections.

After the rabbit antisera had been prepared, purified β-lipoprotein was obtained from several different pools of human plasma (*5*) and the preparations kept separately. They were designated BS1, BS3, and BS0. In one instance the lipid-poor greenish layer, always found at the bottom of the preparative cell after the ultracentrifugal purification of β-lipoprotein, was removed and designated G3 (*4, 5*).

The spectrophotometric method (*10*) for analysis of the specific precipitates was used. Antigen-antibody reaction mixtures, 1.0 ml of an appropriate dilution of antigen added to 1.0 ml of antiserum, were incubated at 37° for 1 hr and then placed at 1° C for 18 hr. Specific precipitates were washed twice with cold saline, being centrifuged for 30 min at 4000 rpm at 0° C to recover the precipitates.

The precipitation curves obtained by reacting pooled rabbit antiserum vs human plasma β-lipoprotein with preparations BS1, BS3, and BS0 are illustrated in Figs. 1 and 2. The curve obtained in the reaction between this antiserum and the lipid-poor fraction, preparation G3, separated during the purification of BS3, is shown in Fig. 2. Since β-lipoprotein has been shown to undergo profound changes on standing (*5*), it should be noted that these preparations were kept at 1° C for various periods of time before first being tested: BS3 and G3 for 1 week, BS1 for 2 weeks, and BS0 for 8 months. That the differences between the precipitation curves of BS1 and BS0 were not due simply to aging and oxidation of the lipoproteins of BS0 is indicated in Fig. 1: BS1 was kept at 1° C for an additional 6 weeks and then retested with the same antiserum. The differences in the BS1 curves on aging would seem hardly enough to account for all the differences between BS1 and BS0. The Tyndall effect of BS1 after 6 weeks had become very intense, indicating that changes had in fact taken place without approaching the immunological characteristics of BS0. It will also be noted that the precipitation curves of BS3 and G3 differed from each other as well as from those obtained with BS1 and BS0.

The supernatants of those reaction mixtures indicated by arrow in Figs. 1 and 2 were tested with the β-lipoprotein preparations by conventional ring tests, and the results are shown in Table 1. The marked heterogeneity of the β-lipoproteins became quite evi-

TABLE 1

THE IMMUNOCHEMICAL HETEROGENEITY OF HUMAN SERUM β-LIPOPROTEIN AS INDICATED BY RING TESTS FOR REACTANTS IN EXCESS

Supernatant tested with	Precipitation curve: antiserum + BS1			Precipitation curve: antiserum + BS0		
	Reaction mixture			Reaction mixture		
	A	B	C	A	B	C
Antiserum	+	+	+	−	+	+
BS1	−	−	−	+	±	−
BS3	+	+	+	−	−	−
BS0	+	+	+	+	−	−
G3	+	+	+	+	−	−
	Precipitation curve: antiserum + BS3			Precipitation curve: antiserum + G3		
Antiserum	+	+	+	+	+	+
BS1	+	+	+	+	+	+
BS3	±	−	−	+	+	+
BS0	+	+	+	+	+	+
G3	+	±	±	±	±	−

dent, and the data substantiated the evidence obtained from the differences in their precipitation curves.

The multiplicity of antigens was also indicated by layering various concentrations of the β-lipoprotein preparations over antiserum in agar according to the Oudin procedure as described by Munoz and Becker (*11*). By this technique 5 bands were readily revealed in BS0 and 6 bands in BS1.

No γ-globulin could be detected in BS1 with rabbit antiserum vs human serum γ-globulin; BS1 contained about 0.2% human serum albumin as determined immunochemically (*10*). The rabbit antiserum vs β-lipoprotein revealed no demonstrable antibodies vs human serum albumin, human serum γ-globulin, or crystallized human serum β-metal-combining globulin (*12*). There was some cross reaction between rabbit anti-β-lipoprotein and the α-lipoprotein fraction, IV-1-1 (*1*), but, owing to the demonstrated heterogeneity of this fraction electrophoretically, this reaction could not be interpreted satisfactorily.

It has been found in this study, therefore, that the β-lipoprotein fraction of normal human plasma represents a class of β-lipoproteins differing in their immunochemical characteristics. Since several preparations of β-lipoprotein obtained from different pools of plasma were studied, the data suggest that the immunochemically reactive components were present in varying ratios in the individual plasmas. The data also indicate that normal human plasma contains a lipid-poor protein that is immunochemically related to the protein moiety of β-lipoprotein; the evidence is insufficient to state this relationship any more positively.

It has been suggested that definite distributions of physical heterogeneity of circulating lipoproteins as demonstrated by the ultracentrifuge is intimately associated with certain pathological states such as atherosclerosis (*6*). The relationships between immunochemical heterogeneity and physical heterogeneity await further investigation, but analysis of the data presented here suggests that immunochemical heterogeneity exists within the various flotation "classes."

The correlation between circulating lipoprotein and human disease is extremely interesting in view of the observation that β-lipoprotein is a component of the cell nuclei of almost all human tissues (*13*). Since the level of individual plasma proteins is a reflection of tissue metabolism, the finding of an altered pattern or level of a particular protein may be only a secondary factor in a disease state rather than a primary or etiologic factor. It is also true, however, that the altered level of the plasma protein, although secondary to tissue metabolism, can itself give rise to characteristic disease as evidenced in hemophilia, afibrinogenemia (*14*), and agammaglobulinemia (*15*). The possible relationships between tissue metabolism and hyperlipoproteinemia in disease await further study.

Kunkel (*16*) fractionated human serum with zephiran and ultracentrifugation and obtained a β-lipoprotein which proved antigenic in rabbits; the rabbit antiserum was then used to estimate lipoproteins in normal and pathological sera. For the estimation of an antigen immunochemically, it must be ascertained that the antigen is either immunochemically homogeneous or that the ratio of its reactive components remains constant. Although the β-lipoprotein employed as an antigen in this study was prepared differently from that of Kunkel, the basic immunochemical criterin for use of antiserum in quantitative estimations were not fulfilled for the β-lipoproteins. By proper absorption techniques, however, it may be entirely feasible to render such antisera specific.

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The Effect of Indoleacetic Acid and Amount of Solar Radiation on Heterosis in the Snapdragon (*Antirrhinum majus* L.)[1]

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In the course of studies with hybrid snapdragons *Antirrhinum majus* L., it became apparent that light was a factor in determining the degree of heterosis and the degree of reaction of the plants to indoleacetic acid. Heterosis is the difference between the mid-parent mean and F_1.

Since auxins are believed to be essential to cell elongation and since one of these substances, indoleacetic acid, is inactivated by riboflavin in the presence of light (*1*), it is possible that a difference in auxin level may account for the phenomenon of heterosis, and that these phenomena may be influenced by the amount of light received by the plant.

In order to test this general hypothesis, two inbred lines of *Antirrhinum majus* L. and their hybrid were chosen as the experimental test subjects. Three experiments were conducted under different light conditions to obtain data on height and dry weight of the parents and of the F_1.

[1] Journal Article No. 1414 of the Michigan Agricultural Experiment Station.

TABLE 1

AV HEIGHT AND DEGREE OF HETEROSIS OF 350 PLANTS EACH OF INBRED (P_1 AND P_2) AND THE HYBRID (F_1) AND SEGREGATING POPULATION (F_2) OF *Antirrhinum majus* GROWN UNDER DIFFERENT AMOUNTS OF LIGHT

Experiment	Total solar radiation (g cal.)	Parent 1 (P_1) height (cm)	Parent 2 (P_2) height (cm)	Mid-parent mean height (cm)	Hybrid (F_1) height (cm)	F_2 height (cm)	Heterosis* height (cm)
I†	5,512.9	7.3	12	9.65	10.38	7.91	0.73
II‡	13,433.8	5.9	8.93	7.415	10.1	9.9	2.685
III§	16,018.1	4.7	9.2	6.95	10.9	6.9	3.95

* Heterosis is the difference between mid-parent mean and F_1.
† Dec. 1, 1951, through Feb. 5, 1952.
‡ Feb. 3, 1952, through Apr. 6, 1952.
§ Mar. 28, 1952, through May 8, 1952.

In order to obtain plants grown under low amounts of light, seeds were sown on December 1, 1951, and 350 seedlings in each group were transplanted 45 days later.

In another trial, under higher amounts of light, seeds were sown on February 2, 1952, and 350 seedlings each (P_1P_2 and F_1) were transplanted on March 28, 1952. In the final test, under still higher amounts of light, seeds were sown on March 28, 1952, and 350 seedlings from each parent were transplanted on April 19, 1952.

The seedlings of the inbreds (P_1 and P_2) and their hybrid (F_1) were grown on a greenhouse bench containing a suitable soil mixture and maintained under uniform greenhouse conditions. Height measurements were made as soon as the tallest population approached 10 cm. Dry weights were recorded after the response to indoleacetic acid was noted.

It was consistently found that heterosis, as detected by these two criteria, increased with seasonal increase in solar radiation as shown in Tables 1 and 2; for example, the degree of heterosis, as measured by dry weight in g/plant, increased from 0.115 under low amounts of light to 0.46 under higher amounts of light.

The plants in the three experiments were sprayed with indoleacetic acid after height measurements were recorded.

Plants grown from December through February under low light conditions were sprayed with indoleacetic acid at 100 ppm and exhibited typical epinasty. However, it was found that on plants grown from March through May, when light intensities were high, a stronger concentration of indoleacetic acid was needed to produce the same degree of response. Concentrations of 1000 ppm were used in the later two trials. Heterotic effect was more evident in the consistently longer and more intense response of the F_1 than in either parent.

TABLE 2

AV DRY WEIGHT IN GRAMS AND DEGREE OF HETEROSIS OF INDIVIDUAL PLANTS OF PARENT 1 (P_1), PARENT 2 (P_2), AND HYBRID (F_1)
(Individual averages based on the av of 350 plants)

Experiment	Parent 1 (P_1)	Parent 2 (P_2)	Mid-parent mean	Hybrid (F_1)	Heterosis*
I†	0.216	0.357	0.286	0.401	0.115
II‡	0.231	0.206	0.216	0.570	0.354
III§	0.12	0.16	0.14	0.6	0.46

* Heterosis is the difference of the F_1 from the mid-parent mean.
† Dec. 1, 1951, through Feb. 5, 1952.
‡ Feb. 3, 1952, through Apr. 6 ,1952.
§ Mar. 28, 1952, through May 8, 1952.

TABLE 3

EFFECT OF A SIMULTANEOUS APPLICATION OF AQUEOUS EXTRACTS OF EITHER P_1 OR P_2 OR F_1 AND INDOLEACETIC ACID AT 25 PPM ON ROOT GROWTH OF CUCUMBER SEEDLINGS
(Seedlings germinated in dark)

Treatment	I Root growth in mm av 16 seedlings	II Root growth in mm av 16 seedlings	Av
Distilled water	5.8	5.5	5.2
IAA*	0.49	1.0	0.74
Parent 1 + 25 ppm IAA*	1.95	2.33	2.14
Parent 2 + 25 ppm IAA*	3.7	4.3	4.00
Hybrid + 25 ppm IAA*	0.47	0.56	0.51

* Indoleacetic acid.

Because the F_1 showed a greater sensitivity to indoleacetic acid, a biological test was employed in an attempt to prove the hypothesis that the F_1 differed from its parents in an indoleacetic-acid-inhibiting or -inactivating mechanism. Alamercery (*2*) has shown that cucumber seedlings are very sensitive to indoleacetic acid. He found that the elongation of hypocotyls and roots is in proportion to the concentration of indoleacetic acid. Accordingly, cucumber seeds were germinated in a distilled water solution of 25 ppm of indoleactic acid with and without a tissue extract of both parents and hybrid snapdragons. The tissue extract was prepared by using a 10-g sample of fresh leaves and stems from the P_1, P_2, and F_1 plants when the F_1 was approximately 10 cm tall. The plants were macerated in a Waring Blendor and made up to a volume of 100 cc. To this slurry indoleacetic acid was

added to make a final concentration of 25 ppm. Sixteen cucumber seeds were placed on a filter paper in a Petri dish and 5 cc of this solution was added to each dish. In addition, a distilled water solution of indoleacetic acid at 25 ppm and distilled water alone were used as controls. Each treatment was replicated five times. The cucumber seedlings were allowed to germinate at constant temperature in darkness. Four days after treatment root measurements were recorded.

It was repeatedly observed that the inhibitory effects of indoleacetic acid on cucumber roots were reduced much less by the extract from the F_1 than by the extracts from either parent. This may suggest that the parents inactivated indoleacetic acid more effectively than did their hybrid (Table 3).

The degree of heterosis in the experimental plants of *Antirrhinum majus* L. was greatly influenced by the amount of solar radiation. Heterotic ability of the F_1 to retain the indoleacetic acid has been demonstrated. The greater ability of the hybrids to retain and utilize growth substance under high light conditions permits greater expansion of plant tissue and thus gives the additional growth increment that can cumulatively result in heterosis.

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The Prevention of Dental Caries by Rock Phosphate in the Diet of the Rat

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The trend toward the fluoridation of communal water supplies offers little for caries prevention in areas where fluoridation of water is impracticable. As a means of supplying extra fluorine in a vehicle other than water, rock phosphate was chosen by us for testing because of its additional high calcium and phosphorus content.

The cariogenic diet, Diet I, which was used contained 800 g cracked yellow corn, 30 g alfalfa meal, 60 g linseed meal, 250 g sucrose, 80 g corn oil, 500 g active dry yeast, and 10 g sodium chloride.

All the caries prevention diets were the same and similar to Diet I except that they also contained Tennessee brown rock phosphate in varying amounts from 5 to 35 g. In several experiments, it was found that the addition of 15 g or less of rock phosphate had little or no caries prevention effect; but above 15 g, the caries prevention effect progressively increased until an optimum effect was reached with approximately 35 g. For this reason the results of only two diets are reported here, namely, Diet II which contained 20 g and Diet III which contained 34 g rock phosphate.

In these experiments 210 Wistar rats were used, one half of each litter being fed one of the diets. The rats were placed on these diets 20–22 days after birth and observed until they died naturally.

Of 105 rats on Diet I, caries appeared in 382 teeth or 61%, mostly lower molars; of 49 rats on Diet II (containing 20 g rock phosphate) caries appeared in 62 or 21% of the lower molars; of 56 rats on Diet III (containing 34 g rock phosphate) caries occurred in 19 or 5% of the lower molars (Table 1).

TABLE 1

Dental Caries in Litter Mate Rats on Diets Containing Brown Rock Phosphate

Diets	No. of rats	Number carious lower molars	Percentage
Diet I	105	382	61
Diet II	49	62	21
Diet III	56	19	5

The upper incisors of the rats on the caries prevention diets were overgrown and curved. Growth lines were seen on many of these teeth. Calcification not only of the jaw bones, but also of the entire skeleton was better in the rats on Diets II and III than in rats on Diet I. The death rate of the rats on the caries prevention diets was normal whereas all the rats on Diet I died between the 4th and 7th months of age.

The rock phosphate used in these diets contains 5.9% calcium fluoride. The concentration of fluorine in Diet II was approximately 350 ppm and in Diet III, it was 700 ppm. Compared to 1–2 ppm of sodium fluoride recommended for use in communal water supplies, this seems like an extraordinarily excessive amount of dietary fluorine for the prevention of caries. But in the rat, it has been established in numerous experiments summarized by Hodge and Sognnaes (*1*) that at least 125–200 ppm of the more soluble sodium salt of fluorine must be present in the rat's diet before an appreciable caries resistant effect can be obtained. Miller (*2*) used 500 ppm dietary calcium fluoride in order to prevent dental caries in the rat. The fluorapatite used in our experimental caries prevention diets is far more insoluble than sodium fluoride, but we preferred to use fluorine in this form because of the extra benefit that might be derived from the additional calcium, phosphorus and other trace minerals present in brown rock phosphate.

Successful cariostasis in the posteruptive phase of dental development as recorded here already has been documented by McClure (*3*).

In experiments on humans, McClendon and Foster (*4*) each ingested daily 2.5 g of rock phosphate containing 75.5 mg of fluorine for three weeks and then reduced the daily intake for three years to 1 g rock phosphate containing 31 mg fluorine. Measuring the

total output of fluorine in the excreta, they calculated a retention of only 1.7 mg/day. More balance studies of this type are needed before safe dosage levels of rock phosphate for human consumption can be considered.

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Synergistic Actions of Carbon Dioxide with DDT in the Central Nervous System

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From clinical observations, physiologic, electroencephalographic, and pathologic studies of cats, monkeys, and dogs, it appears that the cerebellum is the chief portion of the nervous system on which DDT acts (*1, 2*). Histologic degenerative changes resulting from DDT are usually restricted to the cerebellum, especially the dentate and roof nuclei (*1*). Previous investigation of compounds which acted initially on the cerebellum revealed the definite synergistic convulsant activity of the inhalation of carbon dioxide with these compounds (*3*). Accordingly, it was decided to investigate the actions of carbon dioxide on the central nervous system in animals that had ingested DDT.

Thirty-two normal cats, weighing 1.5–3.0 kg, were placed on an ample diet and observed carefully for a week. Then 300–500 mg/kg of DDT, carefully mixed with the diet, was consumed at a single meal. Usually within 24 hr the animals were seen to have generalized, fine tremors and were markedly ataxic. When they were held by the nape of the neck, "running movements" were observed, but no grand mal convulsions were seen. These animals were prepared for acute electroencephalographic recording in the following manner. Under divinyl ether anesthesia, a tracheal cannula was introduced, the femoral veins isolated, and the skull including the area over the cerebellum exposed. Ether anesthesia was then discontinued and paralysis induced with 20 mg/kg of dihydro-β-erythroidine intravenously. Respiration was maintained artificially through a Palmer respirator designed to allow adjustment of stroke volume and rate and the introduction of any desired gas mixture. Screw electrodes were placed bilaterally, 2 over the cerebellum, 2 over the parietal cortex, and 2 over the frontal cortex. Bipolar and monopolar (reference electrode usually on nose) recordings of the electrical activity of the brain and the electrocardiogram were obtained on a Grass 8-channel electroencephalograph. Gas mix-

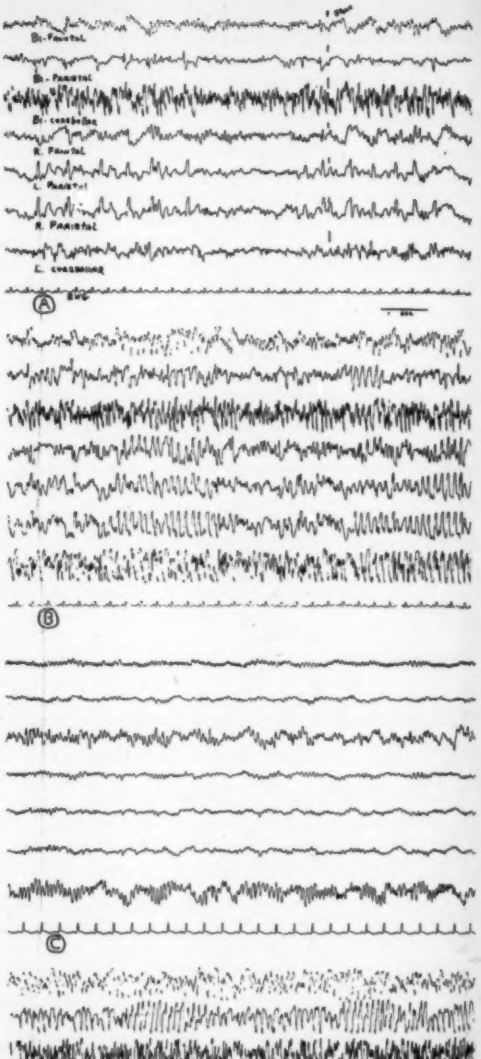

Fig. 1. A. Pre-CO_2 record of a cat that had been fed 400 mg/kg of DDT a day previously. B. Record shortly after the administration of 30% CO_2–70% O_2. C. 30% CO_2–70% O_2 administered for 3 min. D. Record shortly after the removal of the gas mixture.

tures containing 30% CO_2–70% O_2 were obtained commercially.

In all the animals the spontaneous rhythm of the cerebral cortex as well as that from the cerebellum was significantly modified by the ingestion of DDT. The amplitude of the cerebellar activity was markedly increased over that seen in normal control animals. Spikelike waves appeared, although electrical fits were not observed. The cerebral rhythms showed similar activity, but definitely after that seen in the cerebellum (Fig. 1 A). Shortly after the administration of the carbon dioxide mixture (Fig. 1 B), but more usually after its removal, there was marked intensification of all electrical activity, and in eight animals seizures were either observed in the cerebellar leads exclusively or appeared in the cerebellum first and then after a short lag period were also seen in the cerebral cortex. The inhalation of the 30% CO_2–70% O_2 mixture sometimes caused a decrease in amplitude and increase in frequency of the electroencephalogram (Fig. 1 C); however, upon its removal, the typical seizure patterns appeared (Fig. 1 D). In four animals where DDT in doses of 500–1000 mg/kg was ingested, the clinical picture described above appeared 4–6 hr later, and the animals usually died within 12–24 hr after DDT feeding.

Previous work (*4*) showed that high concentrations of carbon dioxide in oxygen increased the frequency but lowered the amplitude of the normal cat EEG. Seizures induced electrically or with Metrazole were antagonized when the gas mixture (30% CO_2–70% O_2) was inhaled. Interestingly, it was found that with Metrazole seizures appeared in the thalamus first and then in the cerebrum (*5*). It is noted that, with convulsants potentiated by carbon dioxide, the fits are either confined to or first seen in the cerebellum and then appear in the cerebral cortex (*3*). This seems to explain the observations on the gross behavior of the animals under the influence of the convulsants and also the histopathology found in the cerebellum. Convulsants antagonized by CO_2 do not show fits first in the cerebellum (*4*).

It is not easy to explain why carbon dioxide can act synergistically with DDT and other cerebellar convulsants. We know that the cerebral cortex can have its threshold for stimulation raised by carbon dioxide. It may be that, once the cerebellar convulsant has been introduced, the additional release from cortical inhibition by carbon dioxide is sufficient to permit seizure activity to start subcortically. The fit is then in turn transmitted to the cerebral cortex. As yet no explanation is offered as to why these seizures start when the CO_2 mixture is first applied or shortly after it is removed. The most likely explanation is that a certain critical level of CO_2 must be maintained for a critical period of time and that this combination of circumstances is sometimes realized during induction with CO_2 and sometimes on the way out.

The oral ingestion of DDT causes gross symptoms of cerebellar involvement. This is also seen when electroencephalographic recordings of cerebral and cerebellar activity are made. Shortly after the introduction or removal of 30% CO_2–70% O_2, definite electrical seizures are seen in the cerebellum exclusively or initially, and later appear in the cerebral leads. This potentiating effect of CO_2 with DDT appears in contrast to the antagonistic actions of CO_2 on seizures induced electrically or with Metrazole.

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Recent Changes in Sea Level Along the New England Coast: New Archaeological Evidence

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Submergence of the Atlantic coast of North America in relation to the tidal plane has long been a problem of interest to geologists, to geographers, to students of plant ecology, and, in more recent years, to archaeologists. Within the past decade archaeological interest has been greatly stimulated by the discovery in New England of extensively submerged aboriginal occupation sites (*1, 2*), and by the striking contrast between past and present tidal conditions in coastal estuaries. Paleobotanical and stratigraphic studies of peat and other plant-bearing sediments found in association with archaeological horizons indicate a progressive encroachment of the sea on shoreline vegetation. These factors, in conjunction with a few recent determinations of the absolute age (*3*) of occupation sites, have focused renewed attention on the problem of coastal stability and its geologic and archaeological implications.

Evidence that has been advanced in the past to demonstrate geologically recent and continuing tidal changes on the Atlantic coast is quite diverse and in part contradictory. Many of the earlier controversies resulted from efforts to prove a priori one theory or another of the geologic consequences resulting from retreat of the Wisconsin ice sheets and subsequent crustal movements of the continental margins. Botanical evidence derived from studies of coastal and estuarine salt marshes and their sedimentary record of peat was variously used to support arguments both for coastal stability and for continued coastal subsidence (*4–6*).

More recently, however, discovery and extensive investigation of the Boylston Street fishweir, a structure excavated at considerable depth in sediments de-

posited in the former Charles River estuary in Boston, show conclusively that submergence of the order of 20 ft has occurred since human occupation of eastern Massachusetts (*7*). Carbon-14 age determinations demonstrate that the time of this human occupation is greater than 3851 (±390) years and less than 5717 (±550) years (*3*). By extrapolation of the two dated levels with the present tidal plane and by assuming the weir itself to be 4500 years old, an average rate of submergence of approximately 6 in. per century may be calculated for the period between construction of the fishweir and European settlement of New England in 1620. These calculations, of course, provide no basis for concluding that the rate of submergence has been constant, nor do they prove definitely that submergence has continued to the present.

Virtual proof of currently continuing and significantly rapid submergence of the Massachusetts coast has been secured, however, from recent archaeological discoveries at Saugus, Massachusetts. Here, in the course of restoring the first successful iron works in North America, by the First Iron Works Association in conjunction with the American Iron and Steel Institute, well-preserved colonial wooden structures have been uncovered at levels now daily inundated by high tides. The arrangement of these structures, which include remains of water wheels, a timbered waterway in its original position, and remnants of a dock and wharf, is such that their intended function would be very inefficient if not impossible under present tidal conditions. Associated with the water wheels and wheel pit timbers are abundant and varied artifacts representing diverse products of colonial manufacture. Owing to the completeness and thoroughness with which the excavation and restoration are being made, it has been possible to make repeated observation of the many physical and cultural features currently exposed at the site. It should be noted, however, that present flooding by the diurnal tide, and especially the effect of occasional excessive tides, are sufficiently greater than they were in colonial time as to render excavating and plotting field relations of buried structures in lower parts of the restoration a difficult engineering problem.

Through the interest and collaboration of Roland W. Robbins, in charge of archaeological investigations at Saugus, precise data concerning present tidal relations have been obtained, as well as useful and important historical information.

Critical examination of the field relations exposed in the Saugus excavation indicates that the entire area of early Iron Works development has been affected since 1650 by an increase in the height of tide in the Saugus estuary of approximately 2½–3 feet. There is no evidence of subsurface slumping, or of localized small-scale deformation of the glacial sediments underlying the site, chiefly sands and gravels interbedded with clays, to account for the change in relation to tidal plane. The operation of shoreline processes that might conceivably have induced localized tidal effects (*5*) has evidently not been a causal factor in submergence at Saugus. The area under consideration is nearly 3 miles from the open sea and is located immediately at the terminus of active drainage of the Saugus River. Seaward from the Iron Works site the present drainage is entirely controlled by tidal action and has quite evidently been influenced by tidal currents since colonial settlement.

Not until archaeological investigation has been completed will it be possible to reconstruct in the desired detail a complete interpretation of the interrelationships between and among the several structures that have been unearthed in the Saugus excavations. Colonial developments there were initiated in a topographic and geographic setting that was apparently selected with careful regard both for its physical features and future development. There is no indication in historical records that the Saugus location proved unsatisfactory from the time of its establishment until activities ceased, except for probable exhaustion of raw materials. Present tidal relationships, however, reveal convincingly that certain features of the Saugus Iron Works could not have been effectively developed and efficiently operated if the tidal range effective today had obtained in 1650.

The Saugus site, although very recent in terms of geologic processes, provides an unusual aggregate of evidence on the question whether submergence of the coast of eastern North America is still continuing. Instrumental records of recent change in the tidal level of the Atlantic and Gulf coastal waters have been analyzed in detail by Marmer (*8, 9*). Results of these studies are of especial interest and strongly confirm by physical measurements the same conclusion; viz., that the eastern coast of the continent is slowly subsiding in relation to present sea level.

Evidence drawn from colonial and pre-colonial archaeological investigation is in such close agreement with that from paleobotanical and geologic studies of coastal change that the controversy over coastal submergence seems finally resolved. There remains to be evaluated, however, the more complex problem of relative effect of eustatic rise in sea level and that of crustal movement in the evolution of the New England coast line.

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A Tissue Derived from the Pollen of *Ginkgo biloba*

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LaRue (*1*) obtained rather remarkable results from the culture of the megagametophytes of *Zamia floridana* and has more recently shown (unpublished) that *Zamia* pollen may develop up to the sperm mother cell stage when grown on a suitable nutrient medium. In the light of this work similar studies *in vitro* were undertaken on *Ginkgo biloba* pollen.

In *Ginkgo,* concurrent with normal development in culture, several types of abnormalities arise. By far the most intriguing aberration is that in which a tissue is initiated from the mass of germinating pollen. Tissue development seems to begin with the production of extra nuclei to give three main types of plurinucleate gametophytes. One finds a coenocytic condition with many nuclei free within the gametophyte (Fig. 1), a multicellular condition at the exine area

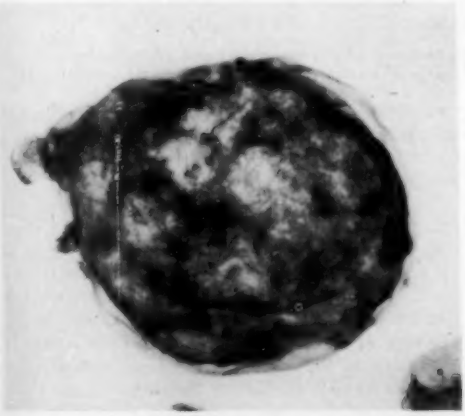

FIG. 1. Coenocytic gametophyte with more than 21 nuclei. Diameter 330 μ.

(Fig. 2), or, infrequently, a several-celled tube or haustorium (Fig. 3). Various stages in the formation of each of these types have been noted in cultures, and as many as 40 nuclei have been seen in the coenocytic gametophytes. It is not known, however, which of the abnormalities has given rise to the pollen tissue. Conceivably, of course, all the abnormalities and the cell types of the gametophyte (prothallial, generative, stalk, body, and tube) could be active in tissue formation. One would, perhaps, expect a prothallial origin, but the indications are strongly against such a hypothesis. One finds little prothallial cell activity in abnormal gametophyte development. Instead, the stalk and tube cells are the most active components. The stalk cell gives rise to the intercalary cells at the exine,

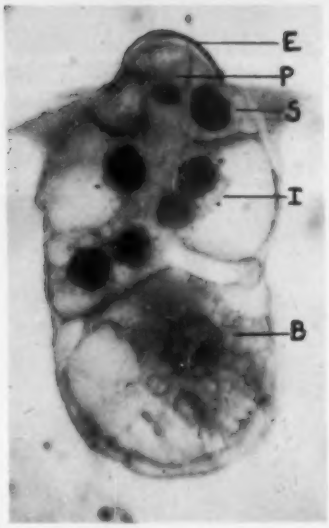

FIG. 2. Intercalary divisions between the so-called "stalk" cell and the "body" cell. E, exine layer of the pollen grain; P, prothallial cell; S, stalk cell; I, intercalated cells and nuclei; B, body cell. Exine diameter approximately 26 μ.

and the tube cell is largely responsible for the septate tubes (Fig. 3) and the coenocytic gametophytes (Fig. 1). Therefore, while both the stalk and tube cells are considered as possible origins of the pollen tissue, the more frequent occurrence of tube-derived abnormalities suggests that the tissue originated from the tube cell of the gametophyte.

The tissue, when first visible macroscopically, appears as a mass of white starch-storing cells arising from the homogeneous mass of germinating pollen. Later, the tissue grows out and may at this time be removed and subcultured. The first tissue mass was isolated on February 2, 1952, and has since passed

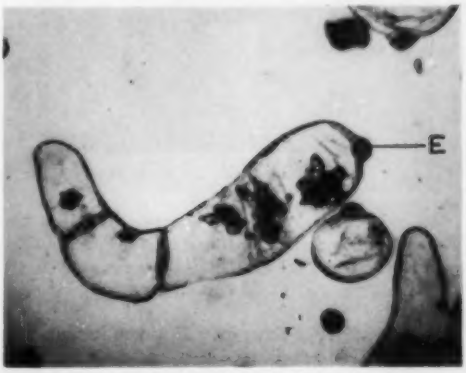

FIG. 3. A three-celled haustorium or tube. The adherent exine at the right is about 26 μ.

through 13 subcultures (Fig. 4). Growth has been most vigorous on a modified White's medium (*2*), to which 0.25% yeast extract and 1 mg IAA have been added per liter. Tissue proliferation continues either on agar or in shake culture at a rate which permits subculturing 1 : 8 in 3 weeks. Moreover, since its establishment as a tissue culture, the pollen tissue has shown no diminution of growth activity.

FIG. 4. *Ginkgo* pollen-derived tissue: this is one month's growth in an 125-ml Erlenmeyer flask; the original inoculum was 5 mm cube. (Natural size.)

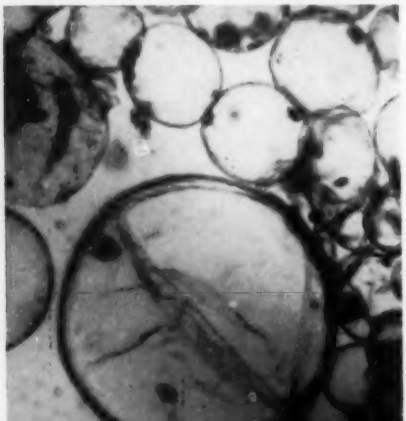

FIG. 5. Vacuolate tissue cells: the giant cell is 483 μ in diameter with clusters of 7 and 3 nuclei.

Ginkgo pollen tissue may be characterized as an undifferentiated, parenchymatous, and often multinucleate cell mass (Fig. 5). The tissue originally has a haploid complement of 12 chromosomes but later becomes polyploid.

Up to the present time, over 25 tissue initials have been observed in a total of 634 culture bottles; this is an incidence of tissue formation of about 4%. Subculturing of many of these initials has resulted in tissue proliferation, although only three such subcultures have been carried on as continuous clones. *Ginkgo* pollen tissue has thus demonstrated, repeatedly, a capacity for potentially unlimited explanation.

Growth *in vitro* of the female gametophyte of *Ginkgo* has also been obtained. In this case, marginal meristems are formed and they produce usually nodular outgrowths. And, although the initial inoculum of the female gametophyte tissue may increase sixfold in volume through marginal proliferation, excision and subculture of the outgrowths have, thus far, not been successful. When grown in light, the tissue not only retains its chlorophyllous nature, but also exhibits a marked increase in the intensity of pigmentation.

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A Report on the Waxy Constituents of Spanish Moss, *Tillandsia usneoides* L.

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Tillandsia usneoides L., commonly called Spanish moss, long moss, crape moss, and Florida moss, is a true epiphyte which festoons trees of swamps and hammocks of the southern coastal states.

The hard, resilient inner fibers are used extensively in the upholstery industry, the remainder of the plant being discarded or utilized as compost. Webber *et al.* (*1*) reported the presence of an antibacterial substance. Mayo Clinic studied the use of moss as a surgical dressing as it is more absorbent than cotton (*2*).

In view of the recent endeavors to procure a suitable substitute for carnauba wax from natural plant sources or by synthesis of low molecular weight waxes (*3*), attention is called to the wax present in commercial quantities in Spanish moss.

In his study on the carbohydrate constituents of Spanish moss, Schroger (*4*) reported the presence of a green-colored wax melting at 79 to 80° C. The presence of this wax was confirmed, and a constituent exhibiting steroidal characteristics was extracted and shown to possess estrogenic activity (*5*). The freshly gathered moss contains approximately 5% wax. The iodine number of this wax is 33.0, the saponification number 120.4, the acid number 25.0, the ester number 95.0, and the melting point 79–80° C.

This wax is soluble in various organic solvents, easily purified, and imparts a hard glossy finish to woodwork and leather, comparable to commercial waxes.

In view of the abundance of Spanish moss, the proximity of the supply and the economy of utilizing

the waste material from the processing of upholstering fibers, it may prove profitable for some industrial organization to investigate this plant as a possible source for a hard natural wax.

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Effects on Plant Growth of Some Compounds with Structural Similarities to Maleic Hydrazide[1]

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Investigation of the effects on plant growth of compounds structurally related to maleic hydrazide should help clarify the mechanism of maleic hydrazide inhibition of plant growth. Maleic acid, maleimide, and the cyclic hydrazides and imides of related dicarboxylic acids should be particularly useful, although other hydrazides, hydrazines, and hydrazine itself might yield information of value. The difficulty of obtaining many of these compounds has been at least partially responsible for lack of reports on their effects on plant growth. This paper deals with the first of a series of experiments on the effects of such compounds on plant growth. Additional compounds in the groups mentioned are being investigated as they become available, not only for comparison with maleic hydrazide, but also for possible interesting effects which they may have on plant growth.

The effects of hydrazine derivatives, other than maleic hydrazide, on plant growth have been investigated little if at all, but there have been a number of studies on the effects of maleic acid and maleates on both plants and animals. Most investigators seem to agree that maleic acid is a respiratory inhibitor in animals and microorganisms, though some have reported it to be utilized as a respiratory substrate (*1, 2*). Annau (*3*) claims that maleic acid competes with fumaric and succinic acids for enzyme surfaces without fulfilling the functions of the latter acids and Weil (*4*) reported that maleic acid inhibits the Krebs cycle but not glycolysis. Copisarow (*5, 6*) found that maleic acid dissolved in etherial oils (but not in water) inhibited the sprouting of potatoes, the ripening of apples, and the growth of fungi on both. Isaacs (*7*) confirmed its effect on fruit ripening, but reported that skin injuries by the acid made the fruits more susceptible to fungi. English *et al.* (*8*) stated that maleic acid is slightly effective as a traumatin. Bonner and Galston (*9*) found that maleic acid had a slight inhibiting effect on plant growth, while Lundegårdh (*10*) reported that maleic as well as fumaric acid was utilized by wheat roots and accelerated their respiration. Thimann and Bonner (*11*) found that maleic as well as other organic acids counteracted iodoacetate growth inhibition. Krishnamurti and Subrahmanyan (*12*) found that maleic acid and a variety of other compounds inactivated the milk-clotting and protease enzymes of fig latex by affecting active —SH groups in the enzymes. Since Greulach and Atchison (*13*) and a number of subsequent investigators have found maleic hydrazide to be an antimitotie in plants, it is particularly interesting that Friedman *et al.* (*14, 15*) found maleic acid to be an antimitotic in chick fibroblasts and later (*16*) reported maleimide and citraconimide to be even more effective antimitotics, whereas succinimide was inactive. They suggest that antimitotic effectiveness was directly proportional to the rate of —SH uptake by these compounds.

Although hydrazides other than maleic have not been used on higher plants, Grunberg and Schnitzer (*17*) and others have found isonicotinic hydrazide and its derivatives to inhibit growth of the tuberculosis bacillus and claim it to be effective in the treatment of tuberculosis.

In the experiments reported on here bean and sunflower plants two weeks old and tomato plants three weeks old were dipped in solutions of the following compounds: maleic hydrazide, maleic acid, diformyl hydrazine, phenylhydrazine hydrochloride, succinic hydrazide, succinimide, isonicotinic hydrazide (rimifon), and 1-isonicotinyl 2-isopropyl hydrazide (marsilid).[2] Succinic and fumaric acids were also used for comparison with possible maleic acid effects, although all three acids were actually applied as their sodium salts to avoid pH effects. With the following exceptions, all solutions were 0.015 *M*: (1) in one experiment with beans 0.03 *M* diformyl hydrazine was used, (2) the quite insoluble succinic hydrazide was applied as a saturated solution of around 3×10^{-4} *M*, (3) succinic hydrazide was also applied to one series of plants at 4000 ppm in lanolin applied to the under surface of one leaf of each plant, with plain lanolin being used on the controls. Dreft was added to each solution at a concentration of 0.025% as a wetting agent. A minimum of six plants was used per treatment, the plants being maintained in a greenhouse in porous clay pots. Weekly observations and measurements of height were made, and "t" values were calculated to determine the significance of the differences of the means.

The effects of the various compounds on the growth

[1] This report is one of a series from a research program aided in part by a grant from the Carnegie Foundation for the Advancement of Teaching.

[2] The maleic hydrazide (as the diethanolamine salt) was supplied through the courtesy of the Naugatuck Chemical Company, the rimifon and marsilid by the Hoffmann-LaRoche Corporation, and the succinic hydrazide, succinimide, and diformyl hydrazine were synthesized by the Chemistry Department of the University of North Carolina under the direction of Arthur Roe.

TABLE 1

MEAN GROWTH OF PLANTS FOR 28 DAYS FOLLOWING TREATMENT WITH COMPOUNDS HAVING AFFINITIES WITH MALEIC HYDRAZIDE

(All solutions were 0.015 *M* except as noted)

Compound	Growth as percentage of growth of controls				
	Beans, 1	Beans, 2	Beans, 3	Tomatoes	Sunflowers
Maleic hydrazide	14.0*	15.2*	15.7*	10.7*	11.7*
Succinic hydrazide solution†	—	53.1*	74.5*	125.2	—
Succinic hydrazide in lanolin‡	—	58.6*	80.0*	139.8‖	—
Diformyl hydrazine§	137.0‖	99.3	74.6*	136.9‖	—
Phenylhydrazine hydrochloride	—	—	3.4*	15.7*	—
Isonicotinic hydrazide (rimifon)	—	—	76.5*	61.0*	93.3
1-Isonicotinyl 2-isopropyl hydrazide (marsilid)	—	—	73.4*	72.9*	60.9*
Succinimide	164.0*	120.7	—	129.1	—
Sodium maleate	185.0*	128.9	—	122.3	—
Sodium succinate	105.0	114.5	—	114.6	—
Sodium fumarate	107.0	115.9	—	125.2	—

* Significant at the 1% level or less.
† About 3×10^{-4} *M*.
‡ 4000 ppm.
§ 0.03 *M* in bean-3 experiment.
‖ Significant at the 5% level.

in height of the plants is summarized in Table 1. Except for phenylhydrazine hydrochloride, none of the compounds caused growth inhibition comparable with that brought about by maleic hydrazide. The phenylhydrazine was apparently quite toxic, causing death of the younger parts of all stems, but subsequent to the time the data in the table were taken, all these plants resumed growth from lateral buds. The new growth was normal except for reduced leaf size. Significant growth inhibition was also caused by succinic hydrazide (in beans but not tomatoes), 0.03 *M* (but not 0.015 *M*) diformyl hydrazine, rimifon, and marsilid. Although inhibition of sunflowers by rimifon 28 days after treatment was not significant, there was a highly significant growth inhibition 14 days after treatment followed by rapid recovery.

Only rimifon and marsilid produced formative effects at all similar to those caused by maleic hydrizide, the marsilid effects being more pronounced in both beans and sunflowers than the rimifon, while neither brought about formative effects in the tomatoes. The principal effects in beans were emarginate leaflet apexes, extra leaflets, and downward curled margins on some leaflets. The sunflower leaf margins were much more extensively curled, many leaves were emarginate, and marsilid reduced leaf size to about half that of comparable control leaves. The leaves which developed subsequent to treatment with marsilid were very narrow, accuminate, wrinkled, and distorted. On many of the older leaves of plants treated with marsilid a roughly oval chlorotic spot developed almost across the base of the blade, and the tissue just above this was unusually dark green. About half of the sunflower plants treated with marsilid lost apical dominance, followed by branching. Marsilid also produced deformities of the flower heads similar to those following maleic hydrazide treatment. Both marsilid and rimifon reduced the number of flowers and fruits of the beans plants significantly, but neither blocked reproductive development as does maleic hydrazide. Succinic hydrazide and phenylhydrazine hydrochloride also reduced but did not block reproductive development of the bean plants.

The leaves of all bean, but not tomato, plants dipped in diformyl hydrazine turned white on the upper surface within a week following treatment, followed by necrotic spots and eventual death of the leaves. Leaves developing subsequent to treatment were not affected. The white surface proved to be due to the loosening of the epidermis from the mesophyll. The bean plants treated with succinic hydrazide looked quite different from those treated with maleic hydrazide, being spindly, generally chlorotic, and somewhat wilted. This indicates that it did not act in a manner comparable with maleic hydrazide, and in view of the low solubility of succinic hydrazide and its failure to affect the tomato plants adversely, it is possible that the effects on beans were due to some other factor, associated with the succinic hydrazide treatments. Further study of this compound is needed.

All plants treated with succinimide, 0.015 *M* diformyl hydrazine, and maleate, as well as with succinate and fumarate, and the tomato plants treated with succinic hydrazide had a greater mean height than the controls, and in the first experiment with beans the differences for maleate and succinimide were highly significant. The plants treated with the compounds mentioned also appeared to be sturdier and darker green than the controls even in experiments in which the differences in height were not significant, indicating that these compounds were being utilized by the plants.

Although the present preliminary data do not warrant any extensive generalizations, they do indicate that further investigation of various hydrazine derivatives as plant growth inhibitors should prove to

be fruitful. On the basis of the results presented here and some of those presented elsewhere, especially by Lundegårdh (*10*), malate (or maleic acid) does not appear to be a plant growth inhibitor, but may actually be utilized by at least some plants. However, in view of the inhibitory effect of maleic acid on animal respiration and mitosis, the possibility that under certain conditions it may act in a similar capacity in plants cannot be discarded. The rather conflicting results with maleic acid could possibly be due to its enzymatic conversion into related naturally occurring metabolic acids in at least some plants under certain conditions.

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The Reduction of Vitamin B_{12}

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We have carried out a titrimetric reduction of cyanocobalamin with chromium (II) ethylenediamine tetraacetate complex in a specific application of a new general analytical technique to be described in detail elsewhere. Here we shall list some observations concerning the nature of reduced vitamin B_{12} which are at variance with those reported by Diehl *et al.* (*1, 2*).

In 0.1 *M* sodium enta, pH 9.5, cyanocobalamin gives a polarogram comprising a single reductive wave, $E_{1/2} = -1.021$ v vs saturated calomel electrode (25°). When this solution is titrated amperometrically with standard 0.1 *N* chromium (II) chloride under rigorous exclusion of oxygen, the diffusion current corresponding to the above wave diminishes linearly with volume of titrant; at the same time an *anodic* wave, $E_{1/2} = -0.311$ v vs saturated calomel electrode appears whose diffusion current reaches maximum development

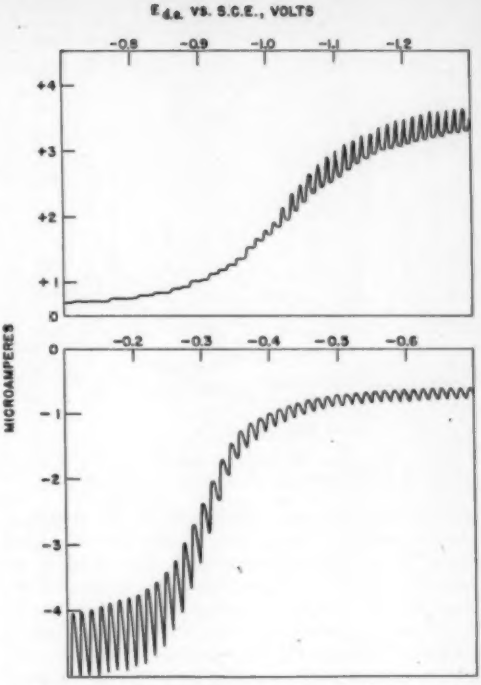

FIG. 1. Top, cathodic wave of vitamin B_{12}; bottom, anodic wave of reduced vitamin B_{12}.

coincident with the vanishment of the cyanocobalamin wave. During this operation the color of the solution changes from red to brown. Polarograms of cyanocobalamin and its reduction product are shown in Fig. 1; titrimetric data on replicate determinations are given in Table 1, and polarographic data in Table 2.

It is evident that cyanocobalamin and its reduction

TABLE 1*

Cyanocobalamin (mg)	Milliequivalents of Cr^{++}	Equivalent weight of cyanocobalamin
13.62	0.01017	1341
2.224	0.001679	1342

* The sample of cyanocobalamin used in this investigation was 99.8% pure by solubility analysis on dry basis; drying loss was 22.8%. All data were obtained on hydrous crystals and corrected accordingly.

TABLE 2

		Cyanocobalamin	Reduction product
$E_{1/2}$ v vs S.C.E.		−1.021 (1.362 mg/cc)	−0.311 (0.3094 mg/cc)
$I_d/Cm^{2/3}t^{1/6}$	(C in mg/cc)	0.219	0.318

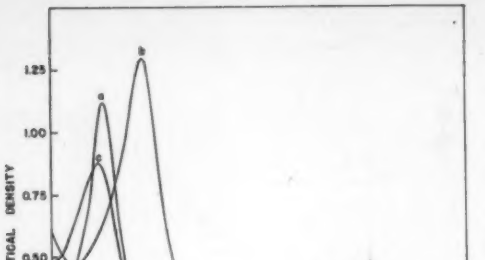

FIG. 2. Absorption spectra: *a*, vitamin B_{12}; *b*, reduced vitamin B_{12}; *c*, air-oxidized product; *d*, $(Cr\ enta)^-$.

product form a system irreversible at the dropping mercury electrode, a situation not unexpected in view of the known loss of cyanide from cyanobalamin on reduction; furthermore, the equivalent weight of cyanocobalamin found by reductive titration corresponds to a 1-electron transfer. The brown reduction product is not oxidized by bromate ion, whereas $(Cr\ enta)^-$ is quantitatively oxidized; however, exposure to oxygen at once eliminates the anodic wave, and the solution turns red. Interestingly, when the air-oxidized material is back-titrated with chromium (II) complex, the solution becomes brown again, but no point can be reached at which an excess of $(Cr\ enta)^-$ is present; apparently the product catalyzes the reduction of water by Cr^{++}.

Diehl (*1, 2*) presents a polarogram obtained on a product termed by him vitamin B_{12r}, produced by reduction of cyanocobalamin with hydrogen on platinum catalyst. Two waves are shown at $E_{1/2} - 0.75$ and -1.37 v vs saturated calomel electrode; although their nature is not specifically defined, they are presumed to be cathodic, by comparison with a polarogram of cyanocobalamin superposed on the graph. This is surprising, because it would be anticipated that a substance having the oxygen avidity of reduced vitamin B_{12} would show anodic depolarization properties, as we indeed found.

The absorption spectra of reduced cyanocobalamin, its air oxidation product, and $(Cr\ enta)^-$ ion at the end point of the titration are illustrated in Fig. 2, with numerical data in Table 3. Again, our reduction product differs radically from that of Diehl, for which absorption maxima are listed at 4730, 4050, and 3125 Å. Since the contribution to the absorption spectrum of reduced cyanocobalamin solution by $(Cr\ enta)^-$ is evidently negligible, the differences are real.

TABLE 3

ABSORPTION MAXIMA OF REDUCED VITAMIN B_{12}

Wavelength (Å)	$E^{1\ cm}_{1\%}$
3853	179
4597	12.5
5537	23.6

Since Diehl reports that his vitamin B_{12r} could be back-titrated with potassium ferricyanide (consuming exactly 1 equivalent), the question is raised whether more than one reduction product of cyanocobalamin is possible. Inspection of Diehl's polarographic data yields some pertinent information. He concludes that the polarographic reduction of cyanocabalamin involves two electrons ($Co^{3+} \rightarrow Co^{+}$) and that of his vitamin B_{12r}, two stages of 1 electron each ($Co^{2+} \rightarrow Co^{+} \rightarrow Co^{0}$). However, his polarograms of cyanocobalamin and vitamin B_{12r} cover almost exactly the same voltage range, a situation difficult to reconcile with the different final valence states of cobalt which are assumed. We have obtained polarograms on various noncrystalline degradation products of vitamin B_{12} which closely resemble that presented by Diehl for vitamin B_{12r}; in this connection, we are informed by E. A. Kaczka that the maximum yield of catalytic reduction products of cyanocobalamin which are regenerable to the starting material approximates 70%. Hence the conclusions of Diehl concerning the identity of his vitamin B_{12r} do not appear justifiable on the basis of evidence which he presents. For the polarographic reduction of cyanocobalamin to a compound of univalent cobalt, no such assessment is possible unless it can be shown that reduction of the organic part of the molecule cannot occur.

In conclusion, the evidence at our disposal indicates that the valence states of cobalt in vitamin B_{12} compounds are the normal 2 and 3, and that in the divalent state the anticipated anodic depolarization properties are present.

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Effect of Toluidine Blue on the Coagulation of Fibrinogen by Thrombin[1]

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Haley and Stolarsky (*1*) pointed out that, although Toluidine Blue was capable of inactivating heparin and decreasing coagulation time *in vitro*, the range

[1] This article is based on work performed under Contract No. AT-04-1-GEN-12 between the Atomic Energy Commission and the University of California at Los Angeles.

within which this action occurred was narrow. Furthermore, beyond a concentration of 25 γ/0.1 ml Toluidine Blue exerted an increasing anticoagulant effect. The complexity of the reactions occurring during coagulation of rabbit plasma did not allow an assessment of the role played by Toluidine Blue in increasing the coagulation time. In an attempt to obtain more information about the influence of Toluidine Blue on the coagulation process, we have investigated its effect on the coagulation of fibrinogen by thrombin. Inasmuch as the results obtained indicate that the dye has a different effect on the purified system than on plasma, it appears that the anticoagulant effect of Toluidine Blue previously reported is not a direct effect on either fibrinogen or thrombin, but it is related to some of the other factors in the coagulation process.

A 1% solution of bovine fibrinogen (Armours, Fraction I, containing 40–50% sodium citrate) in imidazol buffer was prepared as directed by Ware and Seegers (*2*). This solution was kept in a refrigerator overnight and centrifuged before use. Fresh solutions were prepared every 2 days. A stock solution of bovine thrombin (Parke-Davis & Co) containing 100 u/ml was prepared as directed by Ware and Seegers (*2*). A 1:10 dilution of this stock solution was kept in an ice bath before it was made into a working dilution of 1:200. The concentrations of Toluidine Blue in saline were 5, 10, 15, 25, 50, 75, and 100 γ/0.1 ml.

Triplicate tubes containing 0.1 ml of dye and 0.2 ml of fibrinogen solution were set aside for 0, 1, 2, 5, and 10 min prior to the addition of 0.2 ml of 1:200 thrombin. In the second series of experiments the dye and the thrombin were mixed and set aside for 0, 2, 5, and 10 min prior to the addition of the mixture to the fibrinogen solution. Control evaluations employed 0.1 ml of physiological saline instead of the dye solution. The endpoint was the time of first appearance of fibrin threads.

In order to determine if the acidic groups in the fibrinogen reacted with the free primary amine group of the dye, spectrophotometric analyses using the 0.5-cm cell in the Cary Recording Spectrophotometer throughout the range 700 to 220 mμ were made at dye concentrations of 5, 10, 15, 25, and 50 γ/0.1 ml and time intervals of 0, 2, 5, and 10 min. pH determinations of the Toluidine Blue, fibrinogen-Toluidine Blue, and fibrinogen-Toluidine Blue-thrombin solutions were made with the Beckman pH meter.

Figure 1 shows the results obtained at different time intervals when the dye and fibrinogen were mixed first. These results are based upon 9–12 determinations for each point on the curve, and the vertical lines represent the standard deviation. The results obtained when the dye and thrombin were mixed first were practically identical with those obtained when the dye and fibrinogen were mixed first, except that at the 10-min interval all dye concentrations completely inactivated the thrombin and no coagulation occurred. Comparison of the various curves in Fig. 1 shows that those for the 0, 5, and 10 min have a similar shape, with the dye increasing the coagulation time up to the 10- or 15-γ concentrations and then acting as a coagulation accelerator thereafter. The results obtained were not due to changes in pH values because the Toluidine Blue solutions, at the concentrations employed, had values of 6.98–7.0 before mixing with the fibrinogen solution, and a value of 7.0 after mixing. The addi-

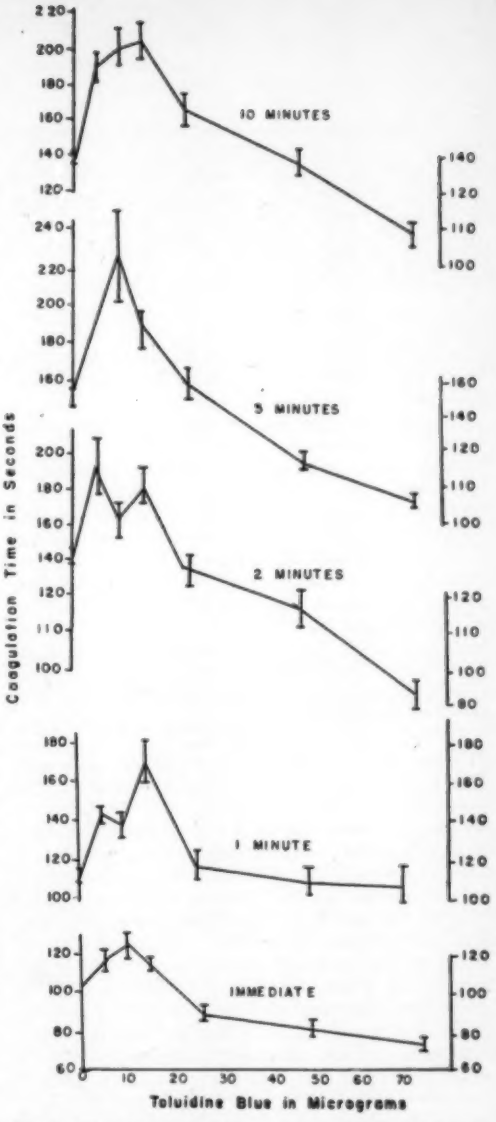

FIG. 1. Effect of Toluidine Blue on coagulation of fibrinogen.

tion of thrombin did not change the pH value of the Toluidine Blue-fibrinogen mixture.

Visible absorption spectra were obtained at all dye concentrations. Absorption spectra were also obtained in the ultraviolet region, but the absorption contribution of fibrinogen was so great at the concentration used in the coagulation studies that accurate measurements were not possible. Toluidine Blue gave a peak at 285 mμ and fibrinogen one at 280 mμ; the combination gave a peak at 282 mμ. The fibrinogen maximum is the same as was previously reported by Waugh and Livingstone (*3*).

The curves for the 1- and 2-min intervals have a similar shape but differ from those of the other time intervals at the 10-γ concentration, where the dye produced a definite acceleration in coagulation. This effect was lost, however, at the 15-γ concentration, where an increased coagulation time was observed. The accelerator effect seen at the 1- and 2-min intervals and at the 10-γ dye concentration cannot be explained on the basis of any effect on the thrombin because, although the dye-fibrinogen and dye-thrombin curves at the 2-min interval and at the 10-γ dye concentration were identical, the thrombin was still active in causing fibrin formations at the other dye concentrations and time intervals. If the thrombin had been inactivated, no fibrin formation would have been detected beyond the 10-γ dye concentration, but such interference with the reaction did not occur except at the 100-γ dye concentration or when the time interval of interaction between the dye and the thrombin was increased to 10 min.

On the other hand, it may have been possible that Toluidine Blue and fibrinogen reacted to form a complex similar to those observed by Michaelis (*4*) for the Toluidine Blue-nucleic acid system. If such were the case, however, definite differences in the absorption spectra of the dye-fibrinogen system would have been apparent in the visible region, and there might have been a definite downward shift in the curve, indicating the presence of the dimeric and polymeric forms of Toluidine Blue. There were, however, no obvious changes in the absorption curve in either the presence or absence of fibrinogen. Furthermore, the curves were identical with the Michaelis (*4*) curves for the monomeric form of Toluidine Blue. These data indicate an additive effect rather than a combination of the two substances. Both the visible and ultraviolet absorption data indicate that the dye and fibrinogen do not form a complex, or, if such a complex is formed, it is a very loose one which does not prevent thrombin from converting fibrinogen into fibrin. Moreover, the coagulation-accelerating action of the dye at the higher dye concentrations might be considered further evidence of no rigid complex formation between the dye and the fibrinogen. Furthermore, the endpoint, fibrin thread formation, cannot be confused with isoelectric precipitation of the fibrinogen because the isoelectric point of fibrinogen is pH 5.4 (*5*), whereas our evaluations were made at pH 7.0. The great differences in the molecular weights of Toluidine Blue (305) and fibrinogen (350,000) (*6*) make it doubtful that additional work using electrophoretic or ultracentrifuge techniques would increase our total knowledge of the reaction taking place. Further investigation must be centered on the other purified components of the blood coagulation system; work on these factors will be reported in detail at a later date.

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The Part Played by Chlorophyll in Plant Transpiration Studied by a New Method: Hygrophotography

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It is known that the transpiration of leaves increases under the effect of light, the first action of which is to cause an increase of the stomatal aperture. The effects of the various spectrum radiations on green leaves are not the same; blue and red radiations, which are precisely those absorbed by chlorophyll, prove to be the most efficient for increasing transpiration. The conclusion arrived at was therefore that light acting upon chlorophyll would thus play an important part in plant transpiration. Van Tieghem (*1*) was even led to assume that in addition to the transpiration function proper of the leaf, as shown by its cells not containing chlorophyll, there also occurred a release of water vapor due to chlorophyll activity, to which he gave the name "chlorovaporization."

This notion of chlorovaporization was not accepted by all botanists, some of whom considered that the phenomenon of chlorovaporization does not occur or if it does occur, causes the vaporization of a very small amount of water which cannot be demonstrated experimentally (*2*).

The hygrophotographic method, which has been described elsewhere (*3*), offers a very sensitive and extremely simple means for definitely solving this problem. This method is based on the use of mercury and silver iodide gelatin photograph films or plates whose preparation has been described and whose properties have been shown (*4*). These plates, which are sensitive to light and normally yellow, blacken rapidly when exposed to light. They are also extremely sensitive to moisture and to water, which instantaneously discolors the plate blackened through exposure. This

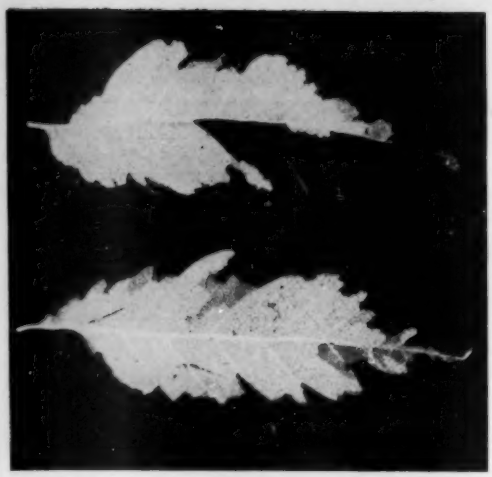

FIG. 1.

FIG. 2.

sensitiveness to moisture is such that it could serve for the study of the *perspiratio insensibilis* of the skin in human physiology and in pharmacology (*5*) and of leaf transpiration in plant physiology (*6*), or to record rains or dew and mist (the last two on spider webs) in meteorology (*7*).

When, in a printing frame a variegated leaf is applied on a hygrophotographic plate preliminarily blackened by exposure, the hygrophotographic image appearing on the plate exactly reproduces, under the effect of transpiration which is more active in the green parts than in the etiolated parts, the contours of the green parts, the yellow areas not yielding any impression on the plate. This phenomenon is quite striking with leaves having an active transpiration such as those of *Acer negundo* (Figs. 1 and 2), *Abutilon savitzii, Tradescantia zebrina,* and marginated leaf of *Pelargonium*. It is not appreciable with coriaceous and evergreen leaves such as those of *Aucuba japonica* or *Evonymus japonicus* the transpiration of which is extremely low.

Figure 1 shows two leaflets of variegated *Acer negundo* photographed by direct lighting of leaflets placed on the sensitive paper; green parts therefore show up in white and etiolated parts in black. Figure 2 represents the hygrophotography of these same leaflets; the green parts, which transpire actively, show up this time in black.

Examination of these images shows that chlorophyll plays an active part in transpiration by promoting the release of water vapor by the leaves.

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Numbers of Fungi and Bacteria in Transatlantic Air[1]

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Aerobiological studies of fungi and bacteria were commenced in 1947 with samples from the Canadian Arctic (*1, 2*). Early qualitative work was supplemented by techniques and apparatus designed for quantitative sampling from rapidly moving aircraft (*3*). Much variation was found in numbers of microorganisms in both temperate and arctic regions which appeared to be correlated with specific air masses (*4, 5*). To obtain further data two flights were made in June and August 1951 from Montreal, Quebec, Canada, to London, England, and return, with RCAF squadron 426 in a North Star (DC-6) aircraft. This is a preliminary report on the numbers of fungi and bacteria obtained from continuous sampling on these two trips, and, as far as the authors are aware, it is the first quantitative study of fungi and bacteria over the Atlantic Ocean.

The samplers were mounted as in previous flights (*3*), and the following samples were taken: 16 filters, 121 sets of plates in the McGill-GE sampler, and 19

[1] This work was supported by grants from the Defence Research Board, Ottawa, Canada.

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[3] The invaluable technical assistance of Sharon Layne and Lucia Kapica is gratefully acknowledged.

TABLE 1

BACTERIA (B) AND FUNGI (F) PER CUBIC FOOT. FLIGHT MONTREAL, QUEBEC, TO LONDON, ENGLAND, WITH STOPOVER AT GOOSE BAY, LABRADOR, JUNE 25–26, 1951, RCAF NORTH STAR. ALTITUDE 9000 FT. FLIGHT DURATION 15 HR 30 MIN. SAMPLES—54

Flight	Air mass			MeGill-GE		Slit		Filter		Fungus spores
	Type	Extent		B	F	B	F	B	F	
		Hr	Min							
Montreal to Goose Bay	Polar(?) continental	3	52					0.025	0.14	6.75
Goose Bay to London	Tropical	1	20	0.2	1.9	0.2	8.2	0.05	0.02	3.7
	Polar	5	10	0.0	0.1	0.05	0.9	0.0	0.01	1.0
	Tropical maritime	3	04	0.07	0.2	0.03	1.1	0.16	0.004	1.5
	Polar(?) maritime	1	28	0.05	0.1	0.05	0.4	0.02	0.006	—

TABLE 2

BACTERIA (B) AND FUNGI (F) PER CUBIC FOOT. RETURN FLIGHT JUNE 29–30, 1951. STOPOVERS AT ST. EVAL, CORNWALL, ENGLAND; KEFLAVIK, ICELAND; GREENWOOD, NOVA SCOTIA. FLIGHT DURATION 16 HR 55 MIN. ALTITUDE 8000 FT. SAMPLES—63

Flight	Air mass			MeGill-GE		Slit		Filter		Fungus spores
	Type	Extent		B	F	B	F	B	F	
		Hr	Min							
London–St. Eval	Tropical	1	07	0.03	4.8	0.56	9.0			
St. Eval–Keflavik	Tropical	5	43	0.26	1.3	0.3	4.4	0.42	0.09	3.0
Keflavik–Greenwood	Tropical	3	00	0.25	0.6	0.26	2.1	0.05	0.02	15.1
	Polar	7	05	0.44	0.14	0.53	0.4	0.02	0.01	0.5
Greenwood–Montreal	No samples taken									

TABLE 3

BACTERIA (B) AND FUNGI (F) PER CUBIC FOOT. SECOND FLIGHT AUGUST 22–23, 1951. MONTREAL TO LONDON, WITH STOPOVER AT GOOSE BAY. FLIGHT DURATION 15 HR 14 MIN. ALTITUDE 9000 FT. SAMPLES—71

Flight	Air mass			MeGill-GE		Slit		Filter		Fungus spores
	Type	Extent		B	F	B	F	B	F	
		Hr	Min							
Montreal to Goose Bay	Polar		30	0.4	1.5	0.2	2.6			
	Tropical or mod. polar	1	46	0.18	1.6	0.3	4.5	0.036	0.26	26.5
	Polar	1	44	0.10	0.6	0.2	2.0	contam	0.05	
Goose Bay to London	Tropical	1	20	0.1	0.7	0.31	6.4	0.02	0.01	2.5
	Polar	6	56	0.03	0.05	0.03	0.2	0.09	0.001	3.9
	Tropical maritime	2	58	0.04	0.2	0.04	1.4	0.03	0.003	1.2

TABLE 4

BACTERIA (B) AND FUNGI (F) PER CUBIC FOOT. RETURN FLIGHT AUGUST 26–27, 1951. STOPOVERS AT PRESTWICK, SCOTLAND, KEFLAVIK, AND GOOSE BAY. FLIGHT DURATION 15 HR 40 MIN. ALTITUDE 8000 FT. SAMPLES—72

Flight	Air mass			MeGill-GE		Slit		Filter		Fungus spores
	Type	Extent		B	F	B	F	B	F	
		Hr	Min							
London to Prestwick	Tropical	1	00	0.39	1.48	1.49	6.1			16.3
Prestwick to Keflavik	Tropical	1	03	0.3	1.1	0.92	8.8			
	Polar	2	35	0.01	0.13	0.19	0.7			0.2
Keflavik to Goose Bay	Polar	7	12	0.03	0.06	0.17	0.5			0.35
Goose Bay to Montreal	Tropical mod.	3	50	0.18	0.5	0.11	0.9			361.4

plates and 25 silicone slides (*6*) in the slit sampler. Exposure length was 1–3 hr for the filters; for all others, 15–30 min over land and 30–60 min over water. Complete data for each sample were obtained from the navigator's log and from the main meteorological office of the Department of Transport at the Dorval Airport at Montreal, Quebec. Averages were made of the numbers of fungi and bacteria in the various air masses by each sampler and are summarized in Tables 1–4. Numbers of bacteria are based on colonies, those of fungi on colonies and numbers of fungus spores.

Wide variation in numbers of fungi and bacteria/cu ft is apparent from these data; it is due in part to the season of the year, the kind of samplers used, and the type of air mass encountered. More organisms were obtained in the August trip (Tables 3, 4) than in the June trip (Tables 1, 2) but the differences were not significant. The samplers varied considerably in their efficiency: for sampling fungi the filters were very inefficient, but for the bacteria, whose numbers with one exception were less than 1/cu ft, the filters were fairly satisfactory. Samples taken over land masses, particularly from Montreal to Goose Bay, had higher numbers than those taken over the ocean.

There was no diminution of organisms in the samples taken over the ocean. Colonies of fungi were present in all plates obtained, confirming the observations of Newman (*7*) over the Pacific Ocean. Bacteria were present in all samples in the August trip; in June, however, some plates had no colonies (Table 1). Fungi were more numerous than bacteria in all samples taken. The numbers obtained over the ocean are probably correlated with air masses. Polar air had very low numbers of both bacteria and fungi, whereas tropical air had higher numbers, with fungi greatly outnumbering bacteria. In one tropical air mass 8.8 fungi/cu ft were recorded from plates exposed in the slit sampler (Table 4).

Silicone slide studies revealed high numbers of fungus spores in the air. Comparison with plate counts clearly indicates the presence of large numbers of spores which are either non-viable or are unable to grow on our media. Concentrations up to 15.1/cu ft were obtained over the ocean (Table 2), and up to 361.4/cu ft over land (Table 4), while in the corresponding plates viable colonies of fungi were less than 1/cu ft. The latter air mass was identified by meteorologists as polar, but the high numbers of fungus spores indicated a tropical continental origin. It is believed that this technique might prove useful in the identification of air masses. Additional information concerning these flights will be published separately (*8*).

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Effect of Fungicidin (Nystatin) in Mice Injected with Lethal Mixtures of Aureomycin and *Candida albicans*

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Seligmann (*1*) recently demonstrated that sublethal doses of *Candida albicans* became highly lethal when mixed with aureomycin. Fungicidin[1] has both strong fungistatic and fungicidal activity *in vitro* against *C. albicans* (*2, 3*); therefore it seemed important to investigate its effect in association with aureomycin since moniliasis is believed by some to be a significant complication of aureomycin therapy.

The fungicidin used for this work was prepared as follows: Methanol extracts of *Streptomyces noursei*[2] mycelia were concentrated *in vacuo*, and the dry residue suspended in a mixture of equal parts of 0.85% sodium chloride solution and butanol. The fungicidin suspended at the interface was collected, washed with saline, and dissolved in methanol by warming at 50–52° C. After chilling, the clarified extract was precipitated with an equal volume of saline. The precipitate was again dissolved in methanol, and the chilled and clarified solution was precipitated by the addition of 4 vol of ethyl acetate. This final precipitate was dried quickly with ether. In cup tests 3.1 μg/ml showed inhibition against *C. albicans*. For *in vivo* tests a fungicidin suspension containing 5 mg/ml was prepared as previously described (*2*). The subcutaneous dose was 0.6 ml.

The strain of *C. albicans* (No. 4657) used in the animal tests was obtained from Rhoda Benham. It was isolated from a case of generalized cutaneous moniliasis. (This culture, since its isolation in 1946, has maintained its high virulence for rabbits: 0.2 ml of a 1:100 suspension in sterile 0.85% sodium chloride solution injected intravenously regularly kills rabbits of 2 to 2.5 kg between the second and third day, with the production of multiple abscesses in the cortex of the kidney.) The growth from a 48-hr culture on Sabouraud's agar slants was washed off with sterile saline and centrifuged at 1500 rpm for 30 min. The packed cells were resuspended in sterile saline (0.1 ml cells plus 2.4 ml saline) (*1*). A dose of 0.2 ml of this suspension corresponded to approximately 100 million viable cells.

[1] The senior authors have given the name Nystatin to their product fungicidin. It is being manufactured by E. R. Squibb and Sons under this name.

[2] Actinomyces No. 48240.

TABLE 1

EFFECT OF FUNGICIDIN (NYSTATIN) IN MICE INJECTED WITH A LETHAL MIXTURE OF *Candida albicans* AND AUREOMYCIN

Material injected	Treatment with fungicidin: No. of doses	Treatment with fungicidin: Time of initial treatment	Results: Deaths*	Results: Time of death (days)	Results: Autopsy findings: Gross lesions +†	Results: Autopsy findings: Gross lesions None	Results: Autopsy findings: Cultural +‡	Results: Autopsy findings: Cultural Unsatisfactory§
C. albicans + aureomycin			10/10	1	5	5	10	
C. albicans + aureomycin	1	At infection	4/10	3–8	4		2	2
" "	10	" "	2/10	2,13		1‖	1‖	
" "	1	4 hr before infection	5/ 5	1–6	4	1	5	
" "	1	2 " " "	1/ 5	12	1		1	
" "	10	2 " " "	1/ 5	3		1		1
" "	1	2 hr after infection	4/ 5	1–3	1	3	3	1
" "	10	2 " " "	2/ 5	2,14		1‖	1‖	
" "	1 or more	4 " " "	10/10	1– 7	3	7	8	2
C. albicans			7/10	2–12	4‖		3	1
Aureomycin			0/10					
Fungicidin			0/10					

The *C. albicans* suspension was administered intraperitoneally in a dose of 0.2 ml containing approximately 100,000,000 viable cells.

The *C. albicans* and aureomycin mixture was administered intraperitoneally in a dose of 0.2 ml containing approximately 100,000,000 viable cells and 1.9 mg of aureomycin.

The aureomycin was administered intraperitoneally in a dose of 0.2 ml containing 2.0 mg.

Fungicidin was administered subcutaneously in doses of 3 mg/0.6 ml, a single dose on the 1st day, two on the 2nd, 3rd, and 4th days, and one on the 5th, 8th, and 9th days.

* Numerator = number of dead mice; denominator = total number of mice.
† Appearance of very small white masses on surfaces of liver, spleen, or kidneys, or on all three organs.
‡ Isolation of *C. albicans* from peritoneal cavity.
§ Examinations unsatisfactory owing to overgrowth with a spreading microorganism.
‖ Remaining mice too decomposed for autopsy.

Crystalline aureomycin was dissolved in sterile saline solution, 10 mg/ml. For the combination of aureomycin and *C. albicans* 2.4 ml of this solution was added to 0.1 ml of packed cells. A dose of 0.2 ml of this mixture contained 100 million cells and 1.9 mg of aureomycin.

Ninety-five white mice (Albany strain) were employed in two separate but similar experiments, 45 mice in one and 50 in the second. Sixty-five were injected intraperitoneally with the mixture of aureomycin and *C. albicans*; 10 were given intraperitoneal injections of the saline suspension of *C. albicans* alone, and 10 aureomycin solution alone; 10 were injected subcutaneously with fungicidin alone.

Of the sixty-five mice injected with the mixture of *C. albicans* and aureomycin, 10 received no fungicidin, and the remaining 55 were divided into groups and treated at different time intervals with single or multiple doses of fungicidin. The mice were observed for 16 days. The results of the two experiments are shown in Table 1.

The 10 mice that received the mixture of aureomycin and *C. albicans* were dead within 24 hr, whereas 7 of the 10 that received *C. albicans* alone survived from 2 to 12 days, and 3 were still alive and appeared well at the end of 16 days.[3] When a single injection of fungicidin (3 mg) was administered 2 hr before infection or at the time of infection, 10 of 15 mice were still alive at the end of 16 days. Subsequent repeated injections of fungicidin did not significantly change the nature of the results. When the administration of fungicidin was delayed until 2 hr after infection, a single dose saved only 1 out of 5 mice, whereas continued treatment saved 3 out of 5. Fungicidin administered 4 hr before or 4 hr after infection showed no protective effect beyond delay in the time of death.

A single dose of fungicidin administered subcutaneously 2 hr before the inoculation of an otherwise lethal mixture of *C. albicans* and aureomycin was highly protective.

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[3] This strain of *C. albicans* is more virulent than that used by Seligmann.

Comments and Communications

Preparation of the Phosphatase Reagent Disodium *p*-Nitrophenyl Phosphate

Bessey and Love (*1*) have recently described a method for the preparation of the disodium salt of *p*-nitrophenyl phosphate which has the advantage of giving a better yield of the salt than the method of Ohmori (*2*). To obtain an essentially pure product, Bessey and Love recommend recrystallization from boiling 87% alcohol and drying over P_2O_5, stating that the preparation becomes yellower with time.

During the development and use of a sensitive method of testing the efficiency of milk pasteurization (*3*), we have gained much experience of this substrate which, for the differentiation of the small amounts of residual phosphatase left in heat-treated milk, must be of a high degree of purity and substantially free of yellow color.

It has been found difficult to obtain colorless crystals of the *p*-nitrophenyl phosphate by methods involving the use of *hot* solvents, such as the recrystallization from boiling 87% alcohol or the precipitation with acetone from solutions in hot aqueous methanol as recommended by Axelrod (*4*). Pure white crystals are more easily obtained by the following modification of Axelrod's purification procedure. The crude disodium salt is dissolved in *cold* 90% methanol at the rate of about 20 ml/g, and an equal volume of acetone is added to the filtered solution. The crystals are filtered off and washed with a volume of acetone equal to that originally added. A second crop of crystals is obtained from the mixture of filtrate and washings. The crystals are spread on filter paper and air-dried.

Disodium *p*-nitrophenyl phosphate crystallizes with 2 molecules of H_2O. It loses this water quite easily, and any loss causes yellowing of the crystals. Actual desiccation should, therefore, be avoided and air-drying of the ether or acetone washed crystals should be considered the method of choice. During and after drying the crystals should be protected from strong light, as this is also detrimental.

In well-stoppered containers, colorless air-dried preparations have been kept in an ice box for several years without visible discoloration. Even at room temperature, little deterioration has been observed after storage for several months, provided that care has been taken to prevent any access of light.

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Documentation

The paper by Raimon L. Beard *et al.* on documentation (Science, 116, 553 [1952]) was read with particular interest. The collecting, classifying, coding and indexing of scientific and technical literature has become so large an undertaking nowadays that it is frightening to think what it will be like in even 10 or 20 years. The only answer lies in some mechanical means of recording this enormous wealth of knowledge. But in the first place this information must be put on to a card, tape, disc, or film and that means a human indexer, since no machine can yet read and understand a scientific paper in a journal.

Dr. Beard's remarks about abstracting journals that ". . . indexing is based on the titles or abstracts, not on the original contribution . . ." is not true of all these journals. Nor is the indexing of the original paper beyond the scope of the abstracting services as he claims it is. Through lack of funds, inadequate support or staffing problems, it is necessary in some organizations to index from an abstract; probably no editor or abstractor will agree that such index entries are as good as those prepared from the original paper.

The ideal index entries must surely be prepared by the individual with a specialist knowledge of the subject matter of the paper, who has read it, written the abstract and is therefore in the best position to know the units and sub-units of thought in the original. This demands a new approach to documentation in that it is the specialist (not an indexer) who does the work of abstracting and indexing, and can thus bring his expert knowledge to bear on both the subject matter for the abstract and the right subject index entries.

This system is not just a hypothetical ideal: it has been in practice very successfully in several centres, and in particular with *Dairy Science Abstracts*. The human indexer who is primarily a specialist is best able to put the proper entries into an index, be it card, tape, disc or film.

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Regarding our paper on documentation (Science, 116, 553 [1952]), such generalities as referred to by Dr. Marsden inevitably lead to exceptions. The abstracting and indexing services merit the highest praise, and the exceptional ones deserve special recognition and encouragement in their efforts to perform an increasingly difficult function.

With the assurance of Dr. Marsden that indexes to abstracts can be prepared in such a way that the important casual observation, incidental to the main theme of a paper, gets recognition, the facilities being tested by the Chemical-Biological Coordination Center offer no advantages over the more conventional ap-

proach—insofar as an indexing system alone is concerned. To this extent, both efforts follow the "growing trend in documentation toward considering units of thought as fundamental . . ." to quote from our paper.

Although the CBCC also calls for specialists to catalog units of thought, the real novelty of its methods lies in the medium of handling the units of thought in such a way that they can be searched from many different points of view, with wide choice as to degree of selectivity, and in simple or complex combinations not possible by any other existing scheme.

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Book Reviews

Geology. O. D. von Engeln and Kenneth E. Caster. New York–London: McGraw-Hill, 1952. 730 pp. Illus. $7.00.

Another in the series of new textbooks in the field of general geology, this book combines the talent of a well-known physical geologist of senior citizenry and the efforts of a paleontologist of established position. The new text, of pleasing appearance, attempts an integration of physical and historical geology into a single unit by interrelated chapters stressing principles of both subjects simultaneously, and avoiding either the artificial separation of physical from historical that is sometimes found, or the repetition necessary in two separate treatments. Throughout, as ideas are presented, relationships to paleontologic and stratigraphic principles are explained.

The text is organized in what is probably correctly termed "the conventional approach." Major headings are (1) "Introduction to Geology," 3 chapters; (2) "The Natural History of Igneous Rocks," 6 chapters; (3) and "Structure, Process, Forms," 13 chapters, which completes the section devoted primarily to physical geology (52% of the 706 pp.). "Geologic History" follows time-scale subdivisions beginning with "Cenozoic Era," 4 chapters; "Mesozoic Era," 3 chapters; "Paleozoic Era," 7 chapters; and "Cryptozoic Eon," 3 chapters. Transition from physical to historical geology is accomplished by closing physical with glaciation, and opening historical with the Pleistocene glacial epoch. It will be interesting to discover, as usage of this text progresses, if the technique of newest to oldest in chronology of historical geology takes any better today than it did in earlier texts similarly constructed.

Few geologists will disagree with the writers that "A basic text in geology should present the subject so as to afford the student . . . inspirational satisfaction," or with their position that the text should also provide a "comprehensive survey of the science to furnish an adequate sound foundation for the advanced courses that comprise the training of the professional geologists." That these two important objectives can be effectively met in the same textbook is an open question. The numerous texts that have appeared in the past 10 years, with only one exception so far as this reviewer is aware, have attempted by monotonously similar techniques to accomplish these objectives. The adding of new texts scarcely seems justified, no matter how sincerely conceived, unless unusual new approaches can be introduced to reach the varied objectives customarily attempted.

The illustrations are well placed and the diagrams attractive.[1] Many are new and original with this book. Some are not as effective as they might be were printing contrasts greater.

The vocabulary of geology is emphasized throughout. Questions for review found at regular intervals whose purpose is defined as permitting "the student to know just what is expected of him in . . . comprehension . . . (and serving) . . . the teacher . . . for tests" could, in this reviewer's opinion, be more imaginative and more commanding of the interrelationships of geological principles, rather than the fact mastery.

Emphasis is placed on reducing the special difficulty of mastering a multitude of technical terms, and it is asserted that "to facilitate attainment of . . . proficiency the explanation of each technical term appears where it is first used." This objective is reached in text, but it would appear that little thought was given when illustrations were inserted, since terms are introduced in subtitles without definition before the concept is introduced in the text, such as in Fig. 39, page 90, where cirque and alluvial fan are introduced, with explanations on pages 112 and 340, respectively, top-set beds, Figs. 50 and 52, pages 109 and 111, and bottom-set beds, Fig. 51, page 110, defined on page 132. Some words new to text treatments, such as "glacierization," are introduced as though they were stock. Some new limitations on common concepts such as restricting magma to plutonic environments, and legalizing "molten lava" for surface magma, appear. This usage may be desirable in modern petrology, but it will probably have limited adoption. A noble effort is found in carefully explaining basic language roots for all technical terms. A few careless statements are evident, such

[1] One important implementation is the recent announcement that a systematic set of 200 colored slides keyed to this text is available from Ward's Natural Science Establishment, Rochester, N. Y.

as (p. 7): "Every crystal is found to fit into one of six systems, each of which is determined by the relations of its *three* axes," but in general the text is remarkably free from such minor incongruities.

The paleogeographic maps are well drawn, although the reproduction might be improved. Use of an overlay transparency, to emphasize the importance of crustal shortening in orogeny since the period to which the paleogeographic condition applied, is commendable, because students rarely make an adequate translation from the geography of the geologic past to the present. It is questionable, however, whether the scale of the overlay and maps will accomplish the desired objective. The presentation of life sequences is unusually interesting, but some will think too much paleontologic and stratigraphic nomenclature is included.

The text gives a well-rounded and adequate presentation which is skillfully woven to make interesting reading. The user will find the text satisfactory, and, where the introductory course is a single unit of both physical and historical geology, the book should be superior to others on the current market.

ROBERT W. WEBB
National Research Council, Washington, D. C.
and *University of California*
Santa Barbara

Scientific Book Register

Metabolic Interrelations: With Special Reference to Calcium. Transactions of the Fourth Conference, January 7–8, 1952, New York. Edward C. Reifenstein, Jr., Ed. New York: Josiah Macy Jr. Fdn., 1952. 262 pp. Illus. $4.50.

Introduction to Evolution. Paul Amos Moody. New York: Harper, 1953. 475 pp. Illus. $6.00.

Wood Chemistry, Vol. 2. American Chemical Society Monograph #97. 2nd ed. Louis E. Wise and Edwin C. Jahn, Eds. New York: Reinhold, 1952. 652 pp. Illus. $15.00.

Biochemistry of Disease (M. Bodansky and O. Bodansky). 2nd ed. Oscar Bodansky. New York: Macmillan, 1952. 1208 pp. Illus. $12.00.

Demand Analysis: A Study in Econometrics. Herman Wold, in association with Lars Juréen. New York: Wiley; Stockholm: Almqvist & Wiksell, 1953. 358 pp. Illus. $7.00.

Rayon Technology (Including Acetate): Handbook for Textile Mills. 2nd ed. Prepared by the Textile Research Department, American Viscose Corp. New York–London: McGraw-Hill, 1953. 344 pp. Illus. $7.00.

Chemical Analysis of Industrial Solvents. Morris B. Jacobs and Leopold Scheflan. New York–London: Interscience, 1953. 501 pp. Illus. $10.00.

Qualitative Analysis and Analytical Chemical Separations. Philip W. West, Maurice M. Vick, and Arthur L. LeRosen. New York: Macmillan, 1953. 223 pp. Illus. $3.75.

Association Affairs

Preliminary Announcement
Seventh Boston Meeting

December 26–31, 1953

Raymond L. Taylor, Associate Administrative Secretary

FROM the programs and other events already arranged, it is apparent that the 120th Meeting of the AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE will be particularly well balanced, well attended, and significant—one of the best meetings in the long annals of the Association. At this time the Association, soon to enter its 106th year, with 238 affiliates and 50,000 individual members, is on the threshold of careful studies to see how its services to science, to scientific organizations, to scientists, and to society may be improved and increased.

One of the fundamental purposes for which the Association was founded, in September, 1848, still endures: ". . . by periodical and migratory meetings, to promote intercourse between those who are cultivating science in different parts of the United States . . ." At Boston this December the annual meeting for the year 1953 once more will bring together leaders and younger men and women in the principal fields of science, not only to read papers reporting current research and to discuss their specialties, but also to attend outstanding symposia and to consider some of the problems that affect science and the world today. This 120th Meeting has as its theme "Scientific Resources for Freedom," and a number of the 18 sections of the Association and participating societies will have programs devoted to physical resources, scientific manpower, and scientific techniques—men, materials, and methods—related to the national economy, security, and welfare.

Although this year's 120th Meeting is typical of AAAS meetings in the past—with national meetings of large societies, interdisciplinary sectional symposia, sessions for contributed papers arranged by many of the sections, distinguished evening addresses, a large-scale Exposition of Science and Industry, and a showing of the latest foreign and domestic scientific films—there is a growing trend toward recurrent conferences in which many scientists, irrespective of their specialties, will be interested. At Boston, in addition to the Academy Conference, representing the 40 academies of science now affiliated with the Association, the Conference on Scientific Editorial Problems II, and the Conference on Scientific Manpower III, there will be one or two sessions on "The Scientist in American Society" and two sessions on "Transmission of Ideas." For the first time in many years, a past president of the British Association for the Advancement of Sci-

ence, Dr. A. V. Hill, will be present and will address the American Association.

AAAS general symposia. The Association will sponsor two general symposia, each of two sessions, in accordance with the decisions of the 1953 Symposium Committee consisting of E. U. Condon, chairman; Frank A. Beach; Bart J. Bok; Charles D. Coryell; A. M. Gaudin; A. Baird Hastings; Jerome C. Hunsaker; James R. Killian, Jr.; Paul C. Mangelsdorf; Philip M. Morse; Alfred C. Redfield; Francis O. Schmitt; Earl P. Stevenson; George B. Wislocki; and Raymond L. Taylor, secretary.

On December 27, the general symposium, "Species Which Feed Mankind," suggested and planned by Paul C. Mangelsdorf will deal with the scientific aspects of several of the critical species of plants and animals that comprise the basic food sources of man. Although the symposium will stress the most recent findings in genetics, plant pathology, and animal husbandry, it is important for all.

On December 29, the second general symposium, "The Sea Frontier," with Alfred C. Redfield and Jerome C. Hunsaker as co-chairmen, will bring together a number of the phenomena of the interface of land and salt water. Aspects included will be the geology of beaches, littoral oceanography, marine ecology, and interrelated engineering and industrial problems.

Focus of the meeting. The activities of the meeting period will center in downtown Boston in the Mechanics Building at 111 Huntington Avenue. Here will be located the Main Registration and Information Center (the only source for special booklets on Boston's points of interest and other literature), the Visible Directory of Registrants, the AAAS Office, the AAAS Science Theatre, and the Annual Exposition of Science and Industry. In the meeting rooms of the building will be held the general symposia and principal sectional programs and, from 8:30 to 11:30 P.M., December 29, the Biologists' Smoker. In nearby Copley Square, the geneticists will occupy the Sheraton Plaza Hotel, and other sessions will utilize auditoria in the Boston Public Library and in Boston University Junior College. Three blocks east of Copley Square, the zoological societies will be based at the Statler Hotel, and two blocks farther, the three science teaching societies will meet in the Hotel Bradford. In Horticultural Hall, three blocks in the opposite direction from Mechanics Building, there will be other sessions. Between the extremes in each direction, the distance is little more than one mile. In general, no one will be more than 5 to 10 minutes away from any other meeting point. Underground trolleys along Huntington Avenue and Boylston Street, with subway connections, will be convenient for those who wish to visit demonstrations or open houses at MIT and Harvard University.

Hotels. The Statler Hotel will be AAAS Headquarters and the locale of such evening events as the Association's Presidential Address, by Detlev W. Bronk, and the AAAS Reception on December 28, and also the annual addresses of the Scientific Research Society of America, the Society of the Sigma Xi, and the United Chapters of Phi Beta Kappa, the dates of which will be announced. Sessions will be held in the Statler (zoologists), the Sheraton Plaza (geneticists), and in the Bradford Hotel (science teachers). Other hotels, to be used primarily for sleeping accommodations, are: the Touraine and Parker House in downtown Boston; the Copley Square, Lenox, and Vendome, near Mechanics Hall; and the Somerset and Kenmore on Commonwealth Avenue in the Back Bay area. Headquarters of each participating society will be given in a later announcement. Detailed housing information and a coupon for room reservations will appear in SCIENCE and THE SCIENTIFIC MONTHLY beginning about the end of July.

Advance registration. As in recent years, advance registrants will receive the General Program-Directory early in December by first-class mail. Coupons will appear in the AAAS journals beginning in late July.

THE PROGRAMS

A—Mathematics

Section A will schedule a vice-presidential address.

B—Physics

Section B will have two symposia; in addition, it will cosponsor with Section M "Transformations within Metallic Crystals" arranged by A. M. Gaudin, and the symposium of Section D; the retiring vice-presidential address, on a subject relating to the upper atmosphere, will be given by O. E. Hulburt. The *American Meteorological Society* will hold a national meeting with two or more sessions for papers.

C—Chemistry

Section C, with Randolph T. Major as program chairman, will have several sessions for contributed papers, principally on Dec. 27, and a six-session symposium "Feeding the Nation": I and II—Human and Animal Nutrition arranged by Robert S. Harris; III—Chemicals in Food, by Charles N. Frey; IV—Chemistry of the Sea as Related to Food Problems, by Harold J. Humm; V—Growth and Nutrition of Plants, by P. W. Zimmerman; VI—Recent Progress in Food Processing, by B. E. Proctor. Appropriate parts will be cosponsored by Sections Nm, G, and O. Dr. Major will give the vice-presidential address. *Alpha Chi Sigma* will schedule a Chemists' Luncheon.

D—Astronomy

Section D will have a comprehensive symposium and panel discussion on "Current Progress in Radio Astronomy" arranged by Bart J. Bok, and a vice-presidential address, "Identifications of Solar Lines," by Charlotte Moore Sitterly, the morning, afternoon, and evening of Dec. 26, in the Lecture Hall of the American Academy of Arts and Sciences.

E—Geology and Geography

Section E is scheduling a two-session symposium in geology and two one-session symposia in geography concurrently on Dec. 28; a two-session symposium,

"Water for Industry," on Dec. 29; and concurrent sessions for contributed papers in geology and geography, Dec. 30 and 31, with appropriate parts of the week's program cosponsored by the *Geological Society of America* and the New England Division, *Association of American Geographers*. The Geologists' Smoker and vice-presidential address by Arthur C. Trowbridge will be the evening of Dec. 30. The *National Speleological Society* will meet the afternoon of Dec. 26.

F—Zoological Sciences

The *American Society of Zoologists* will open four days of sessions Dec. 27 with a symposium, have four concurrent sessions the mornings and afternoons of Dec. 28 and 29, and a second symposium and demonstrations at Harvard on Dec. 30. The Zoologists' Dinner will be on the evening of Dec. 29; an illustrated address will be given by Paul Weiss, vice-president of Section F, which will cosponsor the American Society of Zoologists symposia. The *Herpetologists League* will meet the afternoon of Dec. 28. The recently incorporated *Massachusetts Zoological Society* will have sessions for papers. The *Society of Systematic Zoology* will open four days of meetings with a symposium the evening of Dec. 27, hold sessions for papers, and business meetings the other days.

FG—Zoological and Botanical Sciences

Among the societies whose fields lie in both botany and zoology, the *American Society of Naturalists* this year will hold its annual meeting with the Association with a business session, a symposium, and a presidential address. *Beta Beta Beta* will hold its biennial convention, with an address by Edmund W. Sinnott, executive sessions on Dec. 28, and a luncheon and afternoon session on Dec. 29. The *American Society of Human Genetics* has scheduled three morning sessions for papers, Dec. 28–30; a business meeting, Dec. 28; three afternoon symposia: "Human Genetics and Medical Education," Dec. 28, "Genetic Factors Affecting Intelligence," jointly with the *American Eugenics Society*, Dec. 29, and "Genetics and the Races of Man," cosponsored by the Genetics Society of America, Dec. 30. The annual dinner and presidential address of the society, by C. P. Oliver, will be on the evening of Dec. 29 at the Copley Square Hotel. The sessions of the annual meeting of the *Genetics Society of America* include meetings of the Executive Committee, Dec. 27 and 30; concurrent sessions for papers Dec. 28–30; a luncheon, business meeting, and demonstrations the afternoon of Dec. 29; and the joint symposium "Genetics and the Races of Man," with the American Society of Human Genetics. The *Ecological Society of America* will cosponsor appropriate sessions of Section G and of the American Society of Zoologists and may have a program of its own. The *Society for the Study of Evolution* will have a program at Boston, arranged by Alfred Romer, and it is expected that the *Society for Industrial Microbiology* will again have several days of sessions with the AAAS. The *National Association of Biology Teachers* will hold its annual meeting, Dec. 27–31 with the Association.

G—Botanical Sciences

Section G will have sessions for contributed papers, a number of symposia—including one of two sessions on "Native American Crop Plants and Climatic History in Relation to Man," arranged by Volney Jones and cosponsored by Section H, and one on plant physiology cosponsored by the New England Section of the *American Society of Plant Physiologists*—and a Botanists' Dinner at which Edgar Anderson will give the vice-presidential address.

H—Anthropology

Section H will have a two-session symposium on "Non-Human Primates and Human Evolution" arranged by James A. Gavan, Dec. 27; a symposium on "Theoretical Models for the Study of Cultural Process and Change" by Evon Z. Vogt; the joint symposium with Section G; a group of invited papers on "New England Archaeology" arranged by Douglas Byers, Dec. 29; and sessions for contributed papers, Dec. 29, in the fields of archaeology, social anthropology, etc. The Anthropologists' Dinner and vice-presidential address by Clyde Kluckhohn will be on the evening of Dec. 27.

I—Psychology

The program of Section I includes sessions for invited papers on the areas of learning, comparative behavior, brain function, human engineering, and sensory processes—arranged, respectively, by Fred D. Sheffield, Burton S. Rosner, Walter A. Rosenblith, Leonard C. Mead, and Edwin B. Newman—and for contributed papers, over the period Dec. 28–30. The vice-presidential address will be given on the evening of Dec. 30 by Frank A. Beach.

K—Social and Economic Sciences

Section K has planned two or three two-session symposia, including "Economic Problems of New England," Dec. 27, and "Effects of War on Scientific Development," Dec. 29. The *National Academy of Economics and Political Sciences* will have a symposium cosponsored by Section K and in collaboration with *Pi Gamma Mu*.

L—History and Philosophy of Science

The program of Section L includes a joint symposium, "Art and Science," with the Philosophy of Science Association, on the afternoon of Dec. 27; on Dec. 28 a symposium, "Criteria for Validity in Science" arranged by Philipp G. Frank, cosponsored by the *Institute for the Unity of Science*; and a joint symposium, "Science and General Education," with Section Q and the History of Science Society. The *History of Science Society*, holding its annual meeting with the AAAS, will have a day or two of contributed papers and other events and will cosponsor appropriate symposia of Section L. The *Philosophy of Science Association* will arrange a program for Dec. 30 and cosponsor the symposia of Section L.

M—Engineering

Section M will have a series of symposia: "Aids to the Blind," arranged by Eugene F. Murphy, cosponsored by Sections N and I; "Safety as a Natural Resource"; "The Boston Banks and the Growth Potential of New England" cosponsored by Section P; and the one on metallic crystals referred to under Section B.

N—Medical Sciences

Alpha Epsilon Delta National Premedical Honor Society will hold its annual luncheon Dec. 29. The *American Physiological Society* again will have a symposium under the auspices of the Survey of Physiological Science. The *American Association of Hospital Consultants* will sponsor a symposium on "The Research Function of the Hospital" arranged by E. M. Bluestone; speakers include Jack Masur, Dean A. Clark, and Harvey Agnew, and discussants.

Subsection Nd—Dentistry

Subsection Nd plans three sessions on Dec. 29 arranged by Howard R. Marjerison.

Subsection Nm—Medicine

Subsection Nm will sponsor a four-session symposium "Antimetabolites and Cancer" arranged by Cornelius P. Rhoads and Allan D. Bass, Dec. 28 and 29. The vice-presidential address will be given by Dr. Rhoads.

Subsection Np—Pharmacy

Over the period Dec. 26–31, Subsection Np will have sessions for contributed papers and symposia cosponsored by the Scientific Section of the *American Pharmaceutical Association*, the *American Society of Hospital Pharmacists*, the *American Association of Colleges of Pharmacy*, the *American College of Apothecaries*, the *American Drug Manufacturers' Association*, and the *American Pharmaceutical Manufacturers' Association*.

O—Agriculture

Section O plans some four sessions for Dec. 28 and 29.

P—Industrial Science

Section P, now in its third year, will have a program arranged by Francis J. Curtis. The New England Section of the *American Industrial Hygiene Association* will have a two-day program arranged by W. M. Pierce, consisting of joint meetings with other groups on Dec. 28, a technical session of the society the morning of Dec. 29, and papers of general interest on industrial hygiene, on the afternoon of Dec. 29. (Those interested in giving papers should communicate with F. J. Viles, Jr., Department of Industrial Medicine, MIT.) The *Society for Industrial Microbiology*, it is expected, will have sessions for contributed papers and a symposium, as in prior years.

Q—Education

Section Q plans a two-session symposium on "Visual Efficiency in Industry" and another of three sessions on "Conserving Human Resources," sessions for contributed papers, and a vice-presidential address by Donald D. Durrell, Dec. 28–30. The *AAAS Cooperative Committee on the Teaching of Science and Mathematics* will have a two-session symposium, arranged by George G. Mallinson and cosponsored by Section Q and the three science teaching societies, Dec. 27. The *National Science Teachers Association* will have three days of sessions, a number of them concurrent, others joint with the National Association of Biology Teachers and the American Nature Study Society, Dec. 28–30. The *American Nature Study Society's* annual meeting, from Dec. 26–30, includes a program on marine biology, two sessions on animal ecology, sessions and presidential address, and a joint field trip with the National Association of Biology Teachers.

X—Science in General

The *Committee on Disaster Studies, National Research Council*, is sponsoring the symposium, "Disaster Recovery II," arranged by Harry Williams. The *National Association of Science Writers* will hold its annual meeting with the AAAS and have a program. The *Scientific Research Society of America* and the *Society of the Sigma Xi* will sponsor evening addresses and, on Dec. 29, hold their annual conventions with the Association. The *National Geographic Society* and the *United Chapters of Phi Beta Kappa* will arrange evening addresses.

Call for Papers by AAAS Sections

The following sections of the Association will have sessions for contributed papers. The secretaries or program chairmen to whom titles and brief abstracts should be sent, *not later than September 30, 1953*, follow:

C—Chemistry Dr. Ed. F. Degering, George Washington Inn, New Jersey and C Streets, S.E., Washington, D. C.

E—Geology and Geography Dr. Jack B. Graham, 3400 North Westmoreland Street, Falls Church, Va.

G—Botanical Sciences Dr. Stanley A. Cain, School of Natural Resources, University of Michigan, Ann Arbor, Mich.

H—Anthropology Dr. Gabriel Lasker, Wayne University, 1512 St. Antoine Street, Detroit 26, Mich.

I—Psychology Dr. William D. Neff, Department of Psychology, University of Chicago, Chicago 37, Ill.

Nd—Dentistry Dr. Russell W. Bunting, School of Dentistry, University of Michigan, Ann Arbor, Mich.

Np—Pharmacy Dr. George F. Archambault, Pharmacy Branch, Division of Hospitals, Federal Security Agency, Public Health Service, Washington 25, D. C.

O—Agriculture Dr. C. E. Millar, Department of Soil Science, Michigan State College, East Lansing, Mich.

Q—Education Dr. D. A. Worcester, University of Nebraska, Lincoln, Neb.

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Meetings & Conferences

May 30–31. Society for Investigative Dermatology (Annual). Hotel Belmont Plaza, New York.

June 1–5. American Medical Association (Annual). New York.

June 4–6. Canadian Society of Microbiologists. Ontario Agricultural College, Guelph.

June 4–6. Chemical Institute of Canada (Annual). Prince Edward Hotel, Windsor, Canada.

June 5–6. International Congress of Audiology. Leiden.

June 6–7. International Congress of Bronchology. Utrecht.

June 7–9. American College of Cardiology (Annual). Hotel Statler, Washington, D. C.

June 7–10. American Leather Chemists Association (50th annual). Netherlands Plaza Hotel, Cincinnati, Ohio.

June 8–13. International Congress of Otorhinolaryngology (5th). Amsterdam.

June 9–13. American Dermatological Association. Lake Placid Club, Essex County, N. Y.

June 10–12. Research and Development Associates (Annual). Mayflower Hotel, Washington, D. C.

June 10–20. General Chemistry and Analytical Chemistry Workshop. Pennsylvania State College.

June 11–13. International College of Surgeons. Vienna.

June 12–13. Wilson Ornithological Club. Sheboygan, Wis.

June 12–14. American Medical Technologists (Annual). Hotel Hollenden, Cleveland, Ohio.

June 14–18. American Society of Medical Technologists (Annual). Brown Hotel, Louisville, Ky.

June 14–18. Canadian Gas Association. Windsor Hotel, Montreal.

June 15–17. American Society of Agricultural Engineers (Annual). William Penn Hotel, Pittsburgh.

June 15–17. American Neurological Association (Annual). Hotel Claridge, Atlantic City, N. J.

June 15–18. American Society of Mammalogists. American Museum of Natural History, New York.

June 15–18. American Chemical Society Organic Chemistry Symposium. University of Michigan, Ann Arbor.

June 15–19. American Society of Civil Engineers. Miami Beach, Fla.

June 15–19. Canadian Medical Association (Annual). Winnipeg.

June 15–19. Symposium on Molecular Structure and Spectroscopy. The Ohio State University, Columbus.

June 15–19. American Institute of Electrical Engineers (Summer General). Chalfonte-Haddon Hall, Atlantic City, N. J.

June 15–20. American Association for the Advancement of Science. Pacific Division. Santa Barbara, Calif.

June 15–20. Astronomical Society of the Pacific (with AAAS), Santa Barbara, Calif.

June 15–20. Western Society of Naturalists (with AAAS). Santa Barbara, Calif.

June 15–Sept. 4. Gordon Research Conferences, sponsored by AAAS. Colby Junior College, New London, N. H., and New Hampton School, New Hampton, N. H.

June 16–17. Symposium on Impurity Phenomena. Research Laboratory, General Electric. Schenectady, N. Y.

June 16–18. Division of Physical and Inorganic Chemistry. Summer Symposium. Schenectady, N. Y.

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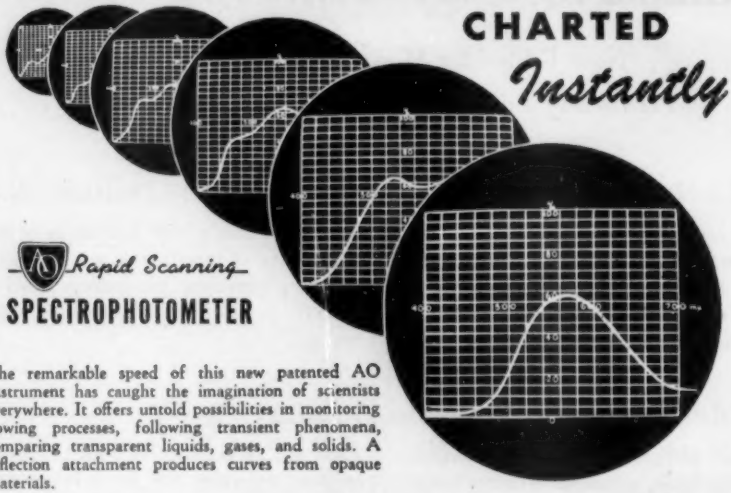

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